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Editorial

Review Articles

Original Articles

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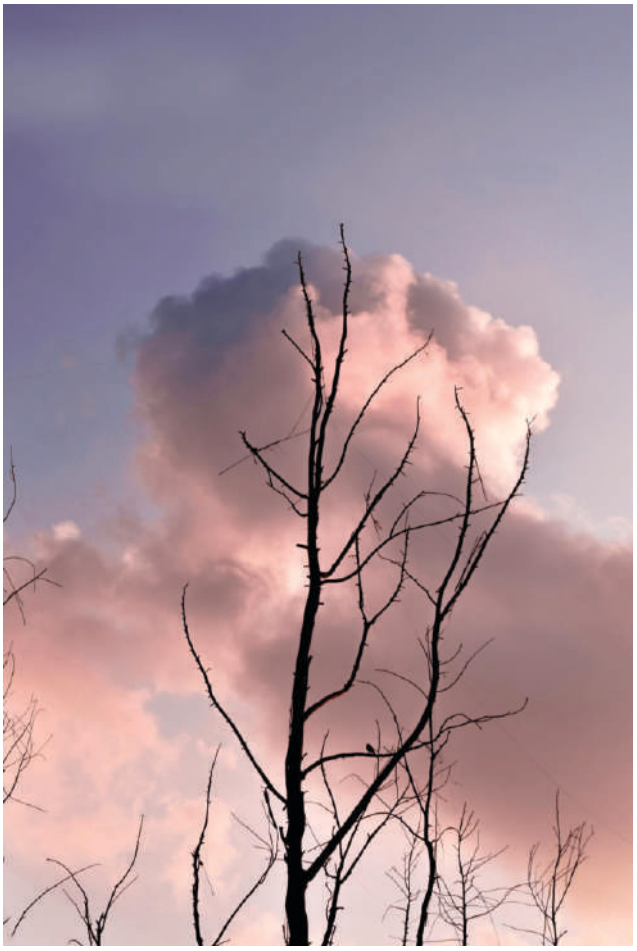
Case Report



Believe that life is worth living and your belief will help create that fact.

Photograph by Ali Rizvi

Pictures on Title

Outstanding Reviewer of Vol. 19, Issue 3 (July – September 2021)

Dr. Sabeen Irshad

Dr. Sabeen is working as Assistant Professor of Pharmacology at Allama Iqbal Medical College, Lahore since 2016 to date. She is a graduate of FJMC, Lahore and completed her M.Phil in Pharmacology from University of Health Sciences, Lahore. She has ten years of teaching experience in Pharmacology. As a student of Pharmacology and research, she believes in continuous professional development through motivation, inquisitiveness, commitment and excellence and seeks to develop new ways of understanding, situating, and reconfiguring knowledge in the telemetric age.

Hope is passion for what is possible.
Photograph by Ali Rizvi

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Battling COVID-19 through Vaccine Hesitancy in Pakistan

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It was one and a half years back, when in January 2020; the first ever sequencing of the Covid-19 virus became public. Since then the scientific community around the world has worked hard to develop various types of vaccines against the pandemic virus, including mRNA, protein, viral vector and other types.[1] Since the efficacy trials of two vaccines had been completed, and have received Emergency Use Authorization (EUA) from the Food and Drug Administration (FDA), other vaccines are also showing up. Pakistan has also developed a vaccine by the name of PakVac. One of the concerns regarding Covid-19 vaccines that havebeen highlighted from the previous studies on SARS and MERS (Middle East Respiratory Syndrome) outbreaks are the possibility of enhancement of the disease by the vaccine. This phenomenon is known as vaccine-associated enhanced disease (VAED).[1,7] Many other issues are still in research regarding the ability of Covid-19 vaccines to mitigate the pandemic. First and foremost is the nature and duration of protective immune response. Secondly, do the minor symptoms after vaccination are attributed to the vaccine itself and thirdly the virus escaping from the protective immune system and long-term follow-up for such rare events needs investigation.

Many conspiracies around the world can be heard about the vaccination against Covid-19, and Pakistan is no exception. Since the declaration of the pandemic almost eighteen months ago, many wild conspiracy theories flourished on social media particularly. Our homeland is vulnerable to such conspiracies and failure of polio eradication programe is one prove to such claims.[3] Vaccine hesitancy is a substantial challenge for Pakistan because of different conspiracies, which starts from certain well known figures in the country down to the individual level, and the over use of social media adding to the hurdles in controlling the continuous waves of the viral pandemic. It's been long since we are in lockdown, full or partial, afraid of the future, as economic turmoil is becoming a burden especially for the developing countries; vaccination is the only way to limit the persisting viral spread.[4] The virus is also mutating continuously with new variant showing up. Some of the major factors contributing towards the slow vaccination process in our country include weak healthcare system, dense population and poor compliance with the practices of hygiene. Pakistan has already experienced a lot of resistance against the polio immunization campaigns; any of the negative perceptions amongst the population towards Covid-19 vaccine would have remarkably devastating effects regarding the efforts in ending the virus.[5]

Government and nation as a whole should get together to implement necessary measures towards speeding up the immunization process in Pakistan. The first major responsibility lies on the media in our country to cope with the ongoing crisis. Electronic and print media must avoid any amplified talks and exaggeration on Covid-19. Television channels must stop airing the discussions on the conspiracy theories.[2,6] Only health professionals must talk on the virus related issues instead of politicians, actors, business figures etc. because harm associated with negative claims must be taken into consideration with great care. Pakistan has seen a big growth in television news channels without a proper check and balance. Social media comments and posts are also part of spreading the conspiracies. The laws are either lacking or if are there, are not strongly implemented. Any person spreading negative claims without any evidence must be held accountable by the law enforcement authorities. Involvement of the local religious authorities may facilitate the vaccination campaign against Covid-19 in our country.[7]

Health authorities and the expanded programe on immunization (EPI) in Pakistan must be fully

involved in the vaccination process by the government, in spreading the positive views and rectifying the misconceptions in the population against the Covid-19 vaccine. It is documented that confidence about vaccines is directly related to the public awareness about the infectious diseases. A huge survey on "attitudes to vaccines" involving 140,000 participants around the world clearly shows that countries with active public-awareness campaigns against different infectious diseases have achieved a very high rates of agreement on vaccine safety, effectiveness, and importance.[8] People are reluctant to be vaccinated because of various claims and religious beliefs about the safety of the vaccine. Inequality, particularly unequal accessibility to all social groups appears to be a more significant obstacle in getting the immunization. There is an utmost need to mobilize community influence, social, print and electronic media awareness for educating the population on Covid-19 vaccination.[9] Accessibility to vaccination center and the availability of proper vaccine is important and especially people going aboard, who need urgent vaccination as a compulsion, ends up in knowing that the vaccine is not available for a while; which makes them frustrated and more negative claims bloom. Government authorities are responsible for looking into the matter as prime importance, so that misunderstandings spread by the media can be controlled.[10]

Adding to the matter is the efficacy of different available vaccines which spreads more misconceptions. People don't understand scientific data, if it gets in the hands of people who are not trained in the field or altogether not educated enough to understand it, rumors spread like fire especially on social media. Vaccines have been developed by international companies and are being administered worldwide. The side effects are yet to be monitored over the years to come, but conspiracy theories are already budding up to the full bloom.[11] Government of Pakistan has authorized the private sector to acquire government-approved vaccines for sale, although no company has yet been able to do so due to a shortage of global vaccine supplies. Incentives to the nation, rather than negative advocacy are the need of the time, as UK and USA have opened many public places, educating their masses to observe SOPs where essential. This can only be achieved if large percentage of population has been vaccinated, or else we would end up in lockdowns, reopening and again closing up, which will affect our economy, education and business in the long run.

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Photograph by ***Ali Rizvi***

AN INSIGHT OF IMMUNOPATHOLOGICAL ASPECTS OF NOVEL CORONA VIRUS AND EXPLORING NEW FRONTIERS IN VACCINE DEVELOPMENT

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Abstract

Coronavirus is a single stranded RNA virus belonging to the Coronaviridae family. The recent corona virus is called COVID-19 that has a ~30 kilo bases genome size similar to other corona viruses. This genome codes for non-structural and structural proteins. The structural protein consists of nucleocapsid (N) protein, membranes protein (M), the spike protein (S) and the envelope protein (E). Since COVID-19 was recently discovered, therefore, there is scant immunological evidence about the virus regarding the antibody or T cell mediated response. Here, we reviewed the structure of COVID-19, the immune mechanism and the pros and cons of available vaccine platforms as well as the options for developing vaccines to accelerate the safe immunization of the global population against COVID-19. Vaccine production is important for limiting harm, return of normal daily routine of the pre - pandemic era and booming of economy.

In Wuhan China, a new highly contagious primary atypical (viral) pneumonia outbreak was noted in December 2019. Since then it is considered to be a zoonotic coronavirus comparable to the Middle East respiratory syndrome (MERS) and severe acute respiratory syndrome (SARS) corona virus and was therefore named as COVID-19.[1]

Coronavirus is a single stranded RNA virus belonging to the Coronaviridae family which infects mostly mammals and birds. In humans, it resembles a simple viral rhinitis. However, few recent human infections of coronavirus have evolved to fatal endemics namely MERS and SARS and 8098 patients of SARS were reported across the globe causing 774 deaths in 2003. The average death rate recorded was 14 – 15%.[2] In 2012, the MERS outbreak occurred in Saudi Arabia during which 2494 patients of MERS were reported worldwide with 858 deaths and an average death rate of (34.4%). The recent COVID-19 belongs to the Beta Coronavirus genus like MERS.[3] COVID-19 has a ~30-kilo bases genome size similar to other coronaviruses. This genome codes for non-structural and structural proteins. The structural protein consists of nucleocapsid (N) protein, membrane-protein (M), the spike protein (S) and the envelope protein (E). Since COVID-19 was discovered there have been several studies on the T cell response and antibodies. Initial findings suggested COVID-19 be fairly related to SARS CoV based upon genome phylogenetic investigation and analogous cell entrance mechanism and human cell receptor usage.[4,5] S protein of coronavirus was reported as an important determinant of the virus for entrance into the host cell.[6] The spike glycoprotein of the envelope fixes to its cell receptor, ACE2 for SARS CoV and SARS COVID-19 , CD209L (also called L-SIGN) for SARS CoV, DPP4 for MERS CoV. The

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entrance of SARS CoV into the cell was mainly considered to be assisted by the direct membrane combination linking the plasma membrane and virus.[7] Most of the SARS CoV studies suggest a protective role for cell mediated as well as humoral immune response. In previous cases, the antibody has been developed in accordance with the virus S protein. In mouse models, the predominant visible protein of SARS Cov demonstrated protection against infection.[8,9] Numerous researches concluded that antibodies developed against the SARS CoV N protein are highly immunogenic that are widely transmitted during the infection were predominantly prevailing in SARS-CoV-infected patients.[10,11] The antibody response came out to be short lived in convalescing patients with SARS-CoV even though it was effective. Long term protection has been shown by T-cell response even up to 11 years after infection. T-Cell response to operational protein turned out to be the greatest immunogenic in peripheral blood mononuclear cells of SARS-CoV patients in contrast to non-structural proteins of all SARS CoV proteins.[12] In addition, the responses of T- cell to S and N proteins were reported to be more frequent and persistent of the structural proteins.[13]

Covid-19 infects macrophages and these macrophages represent corona virus antigen on the surface of T-cell. This process leads to stimulation and differentiation of T-cells which results in the emergence of cytokines linked to variable T-cell subsets (i.e. Th17) accompanied by a significant release of cytokine storm for an increase in the immune response. Owing to the viral perseverance, the continuous development of these mediators has a negative effect on Natural killer (NK) cells and activation of CD-8 T- cells despite the fact that CD-8 T cells produce potent mediators for the destruction of corona virus.[2] Corona virus attachment to DPP4R on the host cell through the S protein triggers the approximation of genomic RNA in the cytoplasm. During partial replication of this virus, the immune response to dsRNA may occur. TLR 3 sensitized dsRNA and signaling pathway cascades (NF-KB and IRF activation, respectively) are triggered to generate pro-inflammatory and Type-I Interferon (IFN) cytokines. Interferon production is important to enhance the release of an antiviral agent to protect the uninfected cells. An excess of corona virus protein may sometimes interfere with the TLR 3 signal and bind to the dsRNA corona virus during infection to inhibit TLR 3 stimulation to escape the immune response. CoV S protein detected by the TLR 4 receptor leads to activation of pro-inflammatory cytokines through the signaling pathway based on MYD88. Virus cell interaction leads to the strong stimulation of immune mediators. As a result of corona virus infection, there is a massive release of chemokine's and cytokines (IL-21, IL-8, IL-6, IL-1, TNF-β, and MCP-1) stimulated by the affected cells. These cytokines as well as chemokines attract leukocytes and lymphocytes to the site of infection.[14-17]

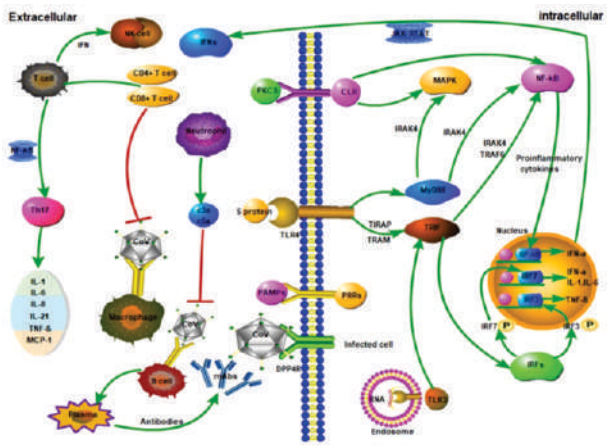

Figure 1: *Green Lines Indicate Activating Effect while Red Lines Refer to Inhibitory Effects.*

The onset of COVID-19 signs and symptoms is usually after an incubation period of about 5.2 days.[18] Duration from the occurrence of symptoms to death is 06 to 41 days with an average of 14 days.[19] The most frequent symptom comprises weakness, cough, and fever with dyspnea, diarrhea, hemoptysis, headache, and sputum production as the usual signs.[20]

COVID-19 vaccine production is a multiplex process comprising of study of the viral genome, receptor target recognition, design, manufacture,

storage and delivery, preclinical and clinical trials. Vaccine production for COVID-19 seems to be a difficult task because of the mutant forms of this novel virus.

Vaccine production and distribution to the common man is an important and urgent need of the hour to control and contain the pandemic. Several organizations across the globe have started developing vaccines depending upon the information procured from SARS and MERS vaccine through various methods such as inactivated COVID-19 virus,[21-23] live attenuated virus, an adenovirus based recombinant vector DNA and RNA vaccine (Figure 2). On 24th of August 2020, WHO acknowledged approximately one hundred and sixty vaccine applicants against COVID-19 out of which at present twenty-six of these vaccines are in clinical phase (Table 1) and one hundred thirty-seven under preclinical assessment.[24] Statistically, 67 percent of natives have to be vaccinated for the prevention and spread of the virus and to gain herd immunity.[25] One of the vaccines that target the COVID-19 spike proteins receptor binding domain (S-RBD) is providing promising results for protective immunity[26] whereas in phase 2/3 human trials, rhesus macaque outcomes after protection and efficacy.[27] On the other hand, 28 days post vaccination (NCT04313127), the ad5 vector COVID-19 aiming at the spike glycoprotein showed immunogenicity.[28] After a single immunization (NCT04341389), the ad5 vectored COVID-19 vaccine at 5/1010 viral particles resulted in a strong immune response in most recipients.[29] Study of two randomized phase 1 and phase 2 inactivated vaccine clinical trials revealed that patients had low side effects and showed immunogenicity (ChiCTR2000031809).[30] Phase half single sighted randomized control trial with adenovirus vaccine demonstrating the COVID-19 spike protein in chimpanzee (ChAdOx1 nCoV19) revealed sufficient safety profile enhanced antibody response.[31] The clinical trial of the mRNA 1273 vaccine demonstrated non-human primate vaccination mediated active neutralizing activity of COVID-19 rapid defense in airways with no pathological changes in the lung fields.[32,33] Step I/II trial of another BNT 162 mRNA based vaccine was conducted in China (ChiCTR2000034825).

During the manufacturing process of live attenuated and inactivated vaccines, proper handling of the virus is a must. On the other hand, recombinant protein and vector based vaccines are safe but require epitope selection, antigen design, and vehicle development. DNA and RNA based vaccines are the two upcoming technologies for the production of COVID-19 vaccine.

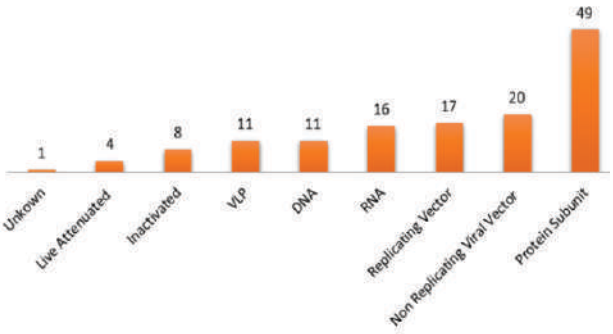

Fig.2: *Distribution of COVID-19 Vaccine Types Underdevelopment. Data modified from W.H.O: https://www.who.int/blueprint/priority-diseases/key-action/novel-coronavirus-landscape-ncov.pdf*

Vaccines are sensitive biological products which may lose potency if exposed to temperatures other

Table 1: *Vaccine in Clinical Evaluation*

Type of candidate vaccine	Developer	Reference
Inactivated + alum	Sinovac	**NCT04456595** NCT04383574 NCT04352608
ChAdOx1-S	University of Oxford/AstraZeneca	ISRCTN89951424 2020-001228-32PACTR20200692 21651322020-001072-15
Adenovirus Type 5 Vector	CanSino Biological Inc./Beijing Institute of Biotechnology	ChiCTR2000031781 ChiCTR2000030906
LNP-encapsulated mRNA	Moderna NIAID	**NCT04405076** **NCT04283461**

DNA plasmid vaccine with electroporation	Inovio Pharmaceuticals/ International Vaccine Institute	**NCT04447781** NCT04336410
DNA plasmid vaccine + Adjuvant	Osaka University/ AnGes/ Takara Bio	**NCT04463472**
DNA plasmid vaccine	Cadila Healthcare Limited	CTRI/2020/07/026352 (not yet recruiting)
Inactivated	Wuhan institute of Biological Products/ Sinopharm	ChiCTR2000031809
Inactivated	Beijing Institute of Biological Products/Sinopharm	ChiCTR2000032459
Whole-Virion Inactivated	Bharat Biotech	CTRI/2020/07/026300
Full length recombinant SARs CoV-2 glycoprotein nanoparticle vaccine adjuvanted with Matrix M	Novavax	NCT04368988
3 LNP-mRNAs	Biotech/Fosum Pharma/Pfizer	2020-001038-36 NCT04368728
DNA Vaccine (GX - 19)	Genexine Consortium	**NCT04445389**
Inactivated	Institute of Medica Biology , Chinese Academy of Medical Sciences	**NCT04412538**
Adeno-based	Gamaleya Research Institute	**NCT04436471** NCT04437875
Native like Trimeric subunit Spike Protein vaccine	Clover Biopharmaceutica ls Inc./GSK/ Dynavax	NCT04405908
Adjuvanted recombinant protein (RBD-Dimer)	Anhui Zhifei Longcom Biopharmaceutical/ Institute of Microbiology, Chinese Academy of Sciences	**NCT04445194**
Recombinant spike protein with Advax™ adjuvant	Vaxine Pty Ltd/Medytox	**NCT04453852**
Molecular clamp stabilized Spike protein	University of Queensland/GSK/ Dynavax	ACTRN1262000067 4932p
LNP-nCoVsaRNA	Imperial College London	**ISRCTN17072692**
mRNA	Curevac	**NCT04449276**
mRNA	People's Liberation Army (PLA) Academy of Military Sciences/ Walvax Biotech.	ChiCTR2000034112
Plant-derived VLP adjuvanted with GSK or Dynavax adjs	Medicago Inc.	**NCT04450004**

than the recommended range.[34] They are sensitive to heat and cold and may lose potency if frozen or exposed to heat or sunlight. Health experts have cautioned that for the effectiveness of vaccine, couple of trials being conducted by various pharmaceutical companies are of view that majority of them especially Pfizer; the recommended temperature for retaining efficacy is minus 70 degrees Celsius or below.

CONCLUSION

COVID-19 infection depends on the interaction between the virus and the individual's immune response. Virulence factors and other associated properties like viral strains, titre, load, mutations play an important role in predicting the host response. Individual immune response also depends upon certain factors like age, physique, nutritional status, gender, genetics (such as HLA genes) and neuroendocrine immune regulation.

Considering the maintenance of cold chain for procurement of vaccine is a tedious task for Pakistan. Intense heat often compounded by poor infrastructure will make it difficult to keep the "cold chain" intact during deliveries to rural areas. So, most of the Asian countries including Pakistan are prioritizing to contain the novel coronavirus rather than looking to stockpile vaccines while others are looking for alternatives to the messenger RNA technology which is being prepared by Pfizer that requires ultra-cold storage for retaining the effectiveness of vaccine. Achieving herd immunity by vaccination is realistic while widespread natural infection continues to be potentially dangerous for humans as well as the economy, unless viral spread induces immunity in far greater fractions of the world population than is actually understood and expected, perhaps in countries with less stringent steps to prevent viral spread. Due to the urgency, coming up with COVID-19 vaccinations and maintenance of cold chain and transport issues must be considered as the top most priority.

Acknowledgments

Not applicable

Limitations of Review

The message could have been more strongly conveyed if the provision of vaccine and cold chain maintenance issues were discussed in detail for Pakistan. But considering the limited data available, we tried our best to address such issue within our capacity.

Conflicts of Interest None

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ANTIMICROBIAL SUSCEPTIBILITY OF TAZOBACTAM AGAINST PSEUDOMONAS SPECIES IN CLINICAL ISOLATES: STUDY FROM A TERTIARY CARE SETTING

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Abstract

Objective: The aim of the study was to provide Antimicrobial Susceptibility of Tazobactam against Pseudomonas species in clinical isolates

Methodology: This cross-sectional study was conducted at Microbiology Department of Allama Iqbal medical college during the period of six months from 1st June to 25th November 2019.Samples were collected from patients admitted in various wards and attending outpatient department and transported to laboratory according to standard protocols. Every specimen received in the Microbiology laboratory was processed according to the recommended protocols for the isolation and identification of bacterial isolates. Pseudomonas were identified by colony morphology, gram staining and biochemical test from the primary isolation plates. A standard Panel of Antimicrobial disks, there concentrations and zone sizes were interpreted according to CLSI 2016 Guidelines.

Results: Of total 675 samples, 370 were gram negative of which P. aureginosa isolation rate was 37.8% (n=140) Lactamase + beta-lactamase inhibitor combination (Piperacillin + Tazobactam) showed very low 14% resistance, against P.aureginosa, while Cefoperazone + sulbactam being similar combination showed 44% resistant.

Conclusion: As antibiotic resistance in Pseudomonas isolates is on the rise, Tazobactum showed very good susceptibility against it as compared to other commonly used antibiotics.

Key Words: Antimicrobial, tazobactam, pseudomonas species

Emergence of drug resistance is one of the alarming issues around the globe.[9] There are multiple factors respon-sible to the emergence of resistance such as, misuse and overuse of antibiotics, inappropriate prescriptions by the physicians, self-medications especially in young adults, use of broad spectrum antibiotics and syner-gistic combinations, un-necessary promotions by pharmaceutical industry, untrained staff in microbio-logical testing laboratories, lack of awareness with the new guidelines recommended for antimicrobial testing etc.[16]

Pseudomonas aeruginosa is one of the major causes of hospital acquired infections especially in patients admitted in ICU (Intensive Care Unit). Data presented by the Center for Disease Control and Prevention(CDC), Nosocomial Infection Surveillance System, in the USA.[6] P.aeruginosa cause diverse variety of infections and was found to be the second most common cause of nosocomial pneumonia, the third most common cause of nosocomial urinary tract infections, and the eighth most common cause of nosocomial bacteremia.[2] (Brigham, Woolverton, Blake, & Staub, 1974). Majority of the infections caused by P.aeruginosa are often severe, life threatening and are untreatable because of the higher resistance to antimicrobial agents and lack of new drugs development. Over all, resistance rates keep

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on increasing and differ according to epide-miology of different geographical locations.[4]

Pseudomonas aeruginosa belongs to a vast genus of obligate aerobic, non-fermenting, saprophytic, Gram-negative bacilli widespread in nature, particularly in moist environments.[8] Most of the cases infected with Pseudomonas comprise of immunocompromised patients including those with burns, cancer or on mechanical ventilation. It can usually be isolated from tap water in clinical settings as well. However these isolates are more resistant to conventional antibiotics as compared to their environmental counterparts. The organism is pathogenic when introduced into areas devoid of normal defenses and infections are both invasive and toxigenic.[10]

Pseudomonas has been incriminated in cases of meningitis, septicemia, pneumonia, ocular and burn infections, hot tubs and whirlpool-associated folliculitis, osteomyelitis, cystic fibrosis-related lung infection, malignant external otitis and urinary tract infections with colonized patients being an important reservoir.[11,15] Cross-transmission from patient to patient may occur via the hands of the health care staff or through contaminated materials and reagents however person to person spread is considered to be rare. Despite recent advances in therapy, P. aeruginosa bacteremia remains fatal in more than 20% of cases. Over 50% of deaths occur within a few days. Therefore, prompt administration of adequate anti-pseudomonas treatment is essential.[6]

Therefore, this study was performed using antibiogram as epidemiological marker to show sensitivity patterns of Psuedomonas aeruginosa against tazobactam at a tertiary care hospital in Lahore.

METHODOLOGY

This cross-sectional study was conducted at Microbiology Department of Allama Iqbal medical college & Jinnah hospital Lahore (AIMC&JHL) during the period of six months from 1st June to 25th November 2019.

Every specimen was processed for bacterial culture for the isolation and identification. Blood agar, chocolate agar, and MacConkey's agar were used. Inoculation was done by four flame streak method. Only single organism P.aureginosa from every specimen was included in the project and processed for further testing. Identification criteria include Colonial morphology, Gram stain, oxidase positive, pyocyanin production. API 20NE was put up for species differentiation

A suspension of P. aureginosa equal to 0.5 McFarland turbidity standards was prepared, by inoculating in nutrient broth. Loning was done by sterile culture swab stick on Mueller– Hinton agar plates according to standard guidelines. A standard Panel of Antimicrobial disks were applied and there Zone sizes were recorded according to CLSI 2016 Guidelines.

RESULTS

Of total 675 samples, 370 were gram negative of which P. aureginosa isolation rate was 37.8% (n=140), Figure: 1

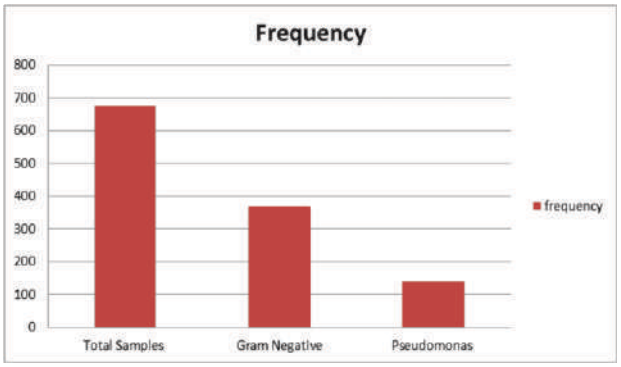

Figure 1: *Frequency of Pseudomonas Aeruginosa*

Table 1 showed department wise distribution of samples & pseudomonas isolates during study

Table 1: *Department-Wise Distribution of Total Samples and P. Aureginosa Isolates*

Location	Samples	Percentage	Isolates	Percentage
ICU	195	28.8	45	32.1
Surgical unit	210	31.1	50	35.7
Medical unit	110	16.2	23	16.4
Gynae	85	12.5	12	8.5
OPD	75	11.1	10	7.1
Total	**675**	**100**	**140**	**100**

period, maximum number of specimens were received from surgical unit 31.1% (n=210/675) followed by ICU 28.8% (n=1950675), Medical unit 16.2% (n= 110/ 675), 12.5% (n=85/675) from Gynae ward, Maximum rate of P. aureginosa was noticed from surgical unit 31.1% (n=50/140)

Among 675 specimens, maximum number of samples were blood (215) and wound swabs (160)

Table 2:Sample Wise Distribution of P. Aureginosa

Sample Type	Total samples	Pseudomonas Percentage
Wound Swab	160	34%
Tracheal aspirate	85	9%
Urine	150	26%
BAL	35	5%
Blood	215	3%
Sputum	30	21%`

and least amount of bronchial alveolar lavage 35 were received,

Table: 2 Frequency of Pseudomonas isolates obtained were as followed, Among 675 samples P. aureginosa was grown in 140 samples, over all maximum number of P. aureginosa isolates were in wound swab 34%, followed by urine 26% sputum 21% least rate found in blood 3%.

Of total 675 samples, 370 were Gram negative, of which P. aureginosa isolation rate was 37.8% (n=

Table 3: Resistant Pattern of Pseudomonas Isolates

Drugs	Resistant
Gentamycin	40%
Meropenem	22%
Imipenem	22%
Cefoperazone+ Sulbactam	44%
Piperacillin +Tazobactum	14%
Ciprofloxacin	43%
Aztreonam	90%
Ceftazidime	65%
Amikacin	67%

140). There was very low resistance in P.aeroguinosa to Lactamase + beta-lactamase inhibitor combination (Piperacillin+Tazobactam) i.e. 14% resistance, while 44% resistance was shown to Cefoperazone + sulbactam being similar combination. Similar resistance rate (43%) was also observed in Fluoroquinolone 2nd generation (ciprofloxacin). Monobactam (Aztreonam), Cephalosporin (Ceftazidime) resistance observed in 90% and 65% isolates respectively. Among aminoglycosides, 67% of isolates showed resistance to Amikacin, while 40% i.e. lower resistance was documented to Gentamycin,as compared to other groups and similar to Carbapenem (Meropenem, Imipenem) 22%, 22% respectively.

DISCUSSION

Infections caused by P. aeruginosa are often severe, life-threatening and are hard to treat because of partial susceptibility to antimicrobial agents and great frequency of emergence of antibiotic resistance through therapy. The antibiotic resistance mechanisms include the acquirement of extended-spectrum-lactamases (ESBL), carbapenems, aminoglycoside-modifying enzymes and 16S ribosomal ribonucleic acid methylases.[11]

Mutational changes causing the up-regulation of multidrug efflux pumps, depression of amp C, modification of antimicrobial targets and changes in the outer membrane permeability barrier are also described. Moreover, the propensity of P. aeruginosa to exist in vivo and in the environment as slow-growing organism embedded in its extracellular matrix adds to its resistance mechanisms. Thus, emergence of MDR in P. aeruginosa is of clinical concern and the pandrug-resistant (PDR) isolates, treatable only with colistin, are on the rise.[8]

P. aeruginosa was isolated in 5.4% cultures. The most common resistance to drugs included Ceclor (100%) and Cefzox followed by 99.6% to Amoxil/ Ampicillin, Cefixime 99.6%, Doxycycline 99.6, Cefuroxime 99.2%, Cephradine 99.2%, Cotrimoxazole 99.2%, Nalidixic acid 98.8%, Pipemidic acid 98.6% and Augmentin 97.6%.[14]

Out of 6280 clinical samples 53.8% yielded significant growth and 9.7% samples were positive for P. aeruginosa out of which 6.8% were nosocomial and 2.9% community-acquired infections. Maximum 67.6% isolates were obtained from pus/swab, followed by urine 15% and blood 4.9%. Elderly, in-patients and

invasive procedures were found to be significant risk factors in the setup investigated (P<0.05). Out of 327 isolates, 84.7% isolates were multidrug-resistant, 35.7%, isolates were extensively drug-resistant. No pandrug-resistant isolate was obtained.[3]

Garba et al reported iso-lation rate, (55%) were Gram-negative organisms and 44 (44%) were Gram-positive.[11] Pseudomonas aerugi-nosa accounted for 25% of the Gram negative orga-nisms. For Pseudomonas isolates, highest sensitivity to Ofloxacin, and moderate susceptibility of Ampicillin, Cefuroxime and Ceftriaxone was observed. Very strong resistance to Cotrimoxazole, Amoxicillin, Tetracycline and Augmentin was observed.[5]

Similarly Khan et al reported The overall drug resistance among 121 strains of P aeruginosa. Very low resistance was observed for Piperacillin- tazobactam (4.9%; P<.05). Meropenem showed significantly high resistance (30.6%; P<.05) as compared to Ticarcillin (22.3%) and Imipenem (19%), Cefepime (8.3%), Amikacin (7.4%) and Pipe-racillin-tazobactam, which showed lowest resistance (4.9%). Although, data varied between hospitals, Meropenem and Ticarcillin had the highest drug resistance in all hospitals. Multidrug resistance was 10.7%.[7]

According to Ali et al, of the 204 Pseudomonas isolates, 39% were obtained from ICU. Overall, 66% were from men, and 17.2% belonged to 10-15 year age group. The overall pattern showed high resistance to Ofloxa-cin 61.3%, Cefepime 57.3%, Ceftazidime 53.9%, Amikacin 53%. Of all the isolates, 63.2% were consi-dered MDR. The most active antibiotics were Colistin, Polymyxin B and Meropenem.[1]

Pathmanathan et al stated that Piperacillin-tazobactam was the most effective drug with 91.8% susceptibility, followed by the Aminoglycosides Amikacin, 86.6% and Gentamicin, 84.5%, the quinolone (Ciprofloxacin), 83.5% and the beta-lactams Cefepime, 80.4%, Cefta-zidime, 80.4%, Imipenem, 79.4% and Meropenem, 77.3% with 19.6% MDR isolates.[12]

Rostamzadeh et al showed extreme antibiotic resistance (99.5%) of P. aeruginosa against against Trimetoprime Sulphamethoxazole and Ciprofloxacin 55.3%, Amikacin 61%, Imipenem 33%.[13]

Khan et al reported the frequency of MDR 30% P. aeruginosa isolated from different clinical specimens. Amikacin was found to be the most effective antibiotic followed by Co-tri-maxazole and Quinolones.[6]

CONCLUSION

Antibiotic resistance in Pseudomonas isolates is on rise. In our study, Tazobactum showed very good susceptibility against Pseudomonas species as compared to other commonly used antibiotics. Therefore, we recommend that tazobactum should be used in patients with Pseudomonas infections, especially in drug resistance cases.

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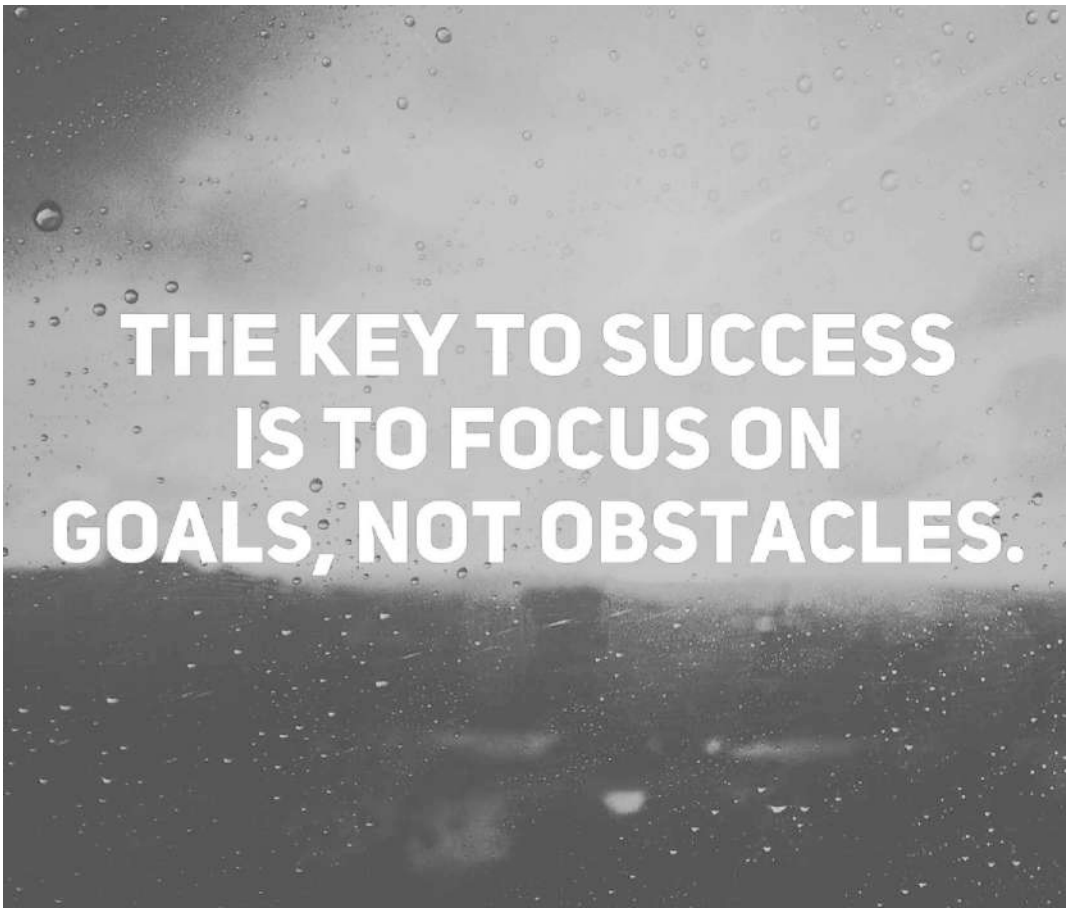

HYPOVITAMINOSIS D INDUCED PROXIMAL MYOPATHY- SIGNIFICANCE OF CLINICAL GROUNDS

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Abstract

Background: Musculoskeletal symptoms can be debilitating, but in developing countries like ours, most of them are due to Vitamin D deficiency, 1 and are reversible as highlighted by our prospective study. Even in setups where the availability of blood investigations for confirmation of diagnosis are unfeasible for various reasons, these symptoms can be assessed clinically and managed timely to avoid delays.

Objective: Our study attempted to evaluate the response of patients to intramuscular vitamin D3 injections on weekly basis and oral calcium supplementation, who had been diagnosed with proximal myopathy and this diagnosis had been confirmed on clinical basis.

Methodology: A cross-sectional prospective study, conducted in two hospital settings, involved patients presenting with complaints of generalized myopathies. Patients below 15 years, above 35 years and those with causes other than hypovitaminosis-D were excluded from our study population.

Results: Initially, we documented complete resolution of body aches followed by a reversal of normal muscle strength within 4 to 6 weeks. Almost all of our patients showed a visible improvement in first 2 to 4 months with symptoms of proximal myopathy being reduced to such low levels in about 6 months which did not interfere with daily life.

Conclusion: Due to patient's affordability issues, clinical evaluation was our mainstay for management and treatment of the patients.

Key words: myopathy, hypovitaminosis D, MRC, muscle power scale, vitamin D3

Focal and diffuse musculoskeletal symptoms are common in patients with metabolic bone disorders.[1,2,3] In patients with cases of vitamin D deficiency (hypovitaminosis-D), the associated muscle weakness has a proximal distribution and variable severity.[3,4] In children with rickets and in adults with established osteomalacia, the muscle weakness can be quite debilitating.[4,6] Homebound older persons are at increa-sed risk for vitamin D deficiency,[7] and the infirmity of old age may conceivably be due, at least in part, to such metabolic factors.[8] In contrast, vitamin D defi-ciency is rarely an obvious etiologic factor when relatively young and active adults have prominent muscle weakness. Diagnostic tests to eliminate other causes of myopathy can be considered but should not be allowed to interfere with the timely correction of vitamin D deficiency.[9] Our experience and studies from the literature are consistent with a good prognosis for myopathic hypovitaminosis-D, although recovery following repletion of vitamin D is slow and variable.

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METHODOLOGY

It was a cross-sectional prospective study done on patients more than or equal to 15 years of age presenting in outdoor clinic from January 2010 to January 2018 at Al Faraz Surgical Hospital and Avicenna Medical College & Hospital, Lahore comp-

laining of difficulty in rising from squatting position, going upstairs and diffuse musculoskeletal pains. Proximal muscle weakness due to other causes were excluded through investigations and clinical evaluation and those taking steroids or indigenous drugs were also excluded. Thus our study included only those patients who were equal to or above 15 years, below 35 years and only those in whom apparent cause of proximal myopathy was hypovitaminosis-D. Vitamin D levels were measured in only two patients, while the rest were treated on the basis of clinical assessment of proximal muscle weakness. These patients were continuously reassessed on weekly follow-ups after supplementation with vitamin D and showed visible improvement after 2 to 6 months. We included 35 cases in our study who presented with proximal myopathy, however we have detailed investigations of only two. Rest of the patients were not investigated due to their affordability issues.

Our first patient was a married female, 21 years of age and mother of a child. When assessed clinically, was unable to stand from squatting position and faced difficulty in raising her lower limbs against mild resistance in supine position. There was no muscle atrophy or tenderness, and deep tendon reflexes were normoactive. Sensation was intact, and her gait was unremarkable. According to the MRC Muscle Power Scale she was put on grade 3 (shown in table). Complete blood counts and serum values for hemoglobin, electrolytes, creatinine, and urea were within normal limits. Serum 25-hydroxyvitamin D3 was low. Based on the clinical presentation and laboratory test results, a diagnosis of vitamin D deficiency due to malnourishment was made. The patient was started on intramuscular vitamin D3, 2 lac International Units (IU) weekly for 6 weeks along with oral calcium supplements 500 mg twice daily

Our second patient who was an unmarried 18 years old female, had to be brought in outdoor due to her inability to walk. When clinically assessed she had grade 2 muscle power in both upper and lower limbs (according to MRC muscle power scale). Her

M.R.C. Muscle Power Scale[10,11]	
Score	**Description**
0	Absence of contraction
1	Traces of contraction
2	Active movement, excluding gravity
3	Active movement with gravity
4	Active movement in presence of some resistance
5	Muscle activation against examiner's full resistance

lab investigations were unremarkable except for serum vitamin D levels which were low.

The rest of the patients between ages 15 to 35, who presented in outdoor with proximal muscle weakness and were unable to stand from squat position were treated on empirical grounds with injection Vitamin D replacements on weekly basis and oral calcium supplements for 6-8 weeks. Improvement was assessed clinically at weekly intervals.

RESULTS

Serum 25-hydroxyvitamin D3 level returned to normal within 2 to 3 months. Muscle strength improved steadily during follow-up examinations; patients were able to rise from the squatting position with steadily increasing speed from about the second month of treatment. Follow-up examination after four months of vitamin D therapy indicated minimal residual proximal muscle weakness, which did not interfere with daily activities and had returned to normal within six months.

DISCUSSION

Various prospective studies showed that the incidence of proximal muscle weakness in patients with diagnosed osteomalacia may be as high as 73%, 6 to 97%,[12]. In studies from the late sixties and early seventies, osteomalacia was diagnosed on the basis of biochemical aberrations (hypocalcemia, hypophosphatemia, increased alkaline phosphatase levels), radiological evidence (evident as wide, transverse lucencies with sclerotic borders traversing partway through a bone, usually perpendicular to the involved cortex; also called Looser zone or pseudo fracture)[13], and bone biopsy specimens (the presence of excessive

osteoid tissue).[6,12] Because of the patient's affordability issues and the unavailability of the precision assays for vitamin D metabolites and intact PTH in serum at the basic clinical laboratories, their diagnosis was made on clinical assessment.

The mechanism of the frequent, and sometimes disabling, muscular weakness that complicates severe vitamin D deficiency is not fully understood. Putative pathophysiologic factors include an ill-defined myopathic process, evident on electromyography studies but not characterized histologically,[6] a neuropathic process associated with secondary hyperparathyroidism,[5] a combined neuro-myopathy syndrome,[12] and a possible defect in vitamin D-mediated calcium transport into myocyte sarcoplasmic reticulum[14]. Notably, both of our patients had readily demonstrable proximal muscle weakness but normal findings on neurologic examination. Similarly, although some myopathic syndromes (Hoffman's Syndrome,[15] in adults and Kocher-Debre-Semelaigne syndrome in children[16] are associated with severe hypothyroidism, subclinical hypothyroidism in patient 1 is an unlikely explanation for her prominent muscle weakness. Thus, a neuropathic mechanism was not clinically evident in our patients, despite the presence of secondary hyperparathyroidism, which has been suggested to induce muscular weakness through a neuropathic process.

Since vitamin D deficiency is the major causes of osteomalacia,[17] the current diagnostic approach emphasizes the measurement of 25-hydroxyvitamin D3 levels together with relevant biochemical indices. X-ray film studies are useful for documenting pseudo fractures and other deformities; bone biopsy, however, is rarely done for the routine diagnosis of osteomalacia[18]. The incidence of muscle weakness in patients with vitamin D deficiency without the skeletal hallmarks of osteomalacia or rickets is unknown, but it may well be substantial. The presence of osteomalacia apparently is not necessary for the development of muscle weakness in persons with vitamin D deficiency.[19]

In scenarios similar to our setting where affordability dictates the methodologies for evaluating, diagnosing and treating patients, clinical grounds prevail over other methods. To be able to do that, MRS scale (Oxford Scale) despite of its limitations, is widely acceptable for evaluating muscle strength.[20] This test involves testing the muscle strength of both upper and lower limb, and be able to grade them 0-5 according to the scale. In addition to grading muscle strength, it can also be used to assess the outcome of the treatment. In such a patient, an early therapeutic trial of vitamin D is warranted. The ultimate proof of the diagnosis of vitamin D-deficient muscle weakness rests on the response to therapy. Improvement in muscle strength has been observed as early as after a week,[6] but usually within one to two months,[9,21] of treatment with pharmacologic doses of vitamin D. However, for a complete recovery of muscle strength, treatment is required for several months.[4,9]

Some authors have reported a pattern of incomplete recovery, as evidenced by persistent deficit in maximum voluntary isometric quadriceps strength during follow-up on long-term vitamin D therapy.[19] We found the "squat-stand" timing test to be a useful semi quantitative bedside method of observing proximal muscle strength. Initially, weak patients were unable to stand from the squatting position and were assigned the worst baseline "squat-stand" time of infinity. Following appropriate treatment, patients were able to rise (albeit slowly) from a squatting position. The time needed to reach a fully upright posture, recorded as part of the follow-up office notes, was inversely related to the proximal muscle strength. A lack of objective improvement in proximal muscle strength (documented by "squat-stand" times) after about a month on an adequate dosage of vitamin D indicates a need for reevaluation of the diagnosis.

CONCLUSION

Muscle weakness is common among vitamin-D deficient individuals. Our study indicates that more focus should be placed on muscle symptoms,[22] in at-

risk population groups especially in setups where blood investigations for confirmation of diagnosis are not readily available. Our approach in assessing and treating patients readily on clinical grounds proved to be beneficial amongst non-affording patients.

Even though the rest of the world has advanced to more modern methods in managing such scenarios, but given our situation, we stuck with pragmatic methods that are now almost obsolete. The patients were advised to undergo extensive and expensive lab workups on their previous visits to clinicians, overlooking their clinical significance and socioeconomic status.

By simply using the MRC scale we were able to grade their strength initially and monitor their response to treatment over the course of time, efficiently and economically. The vitamin D deficiency related myopathy should not be missed due to its potential reversibility with vitamin D supplementation.

Limitations of study

The main concern throughout, was the affordability of the patients that prevented them from undergoing costly investigations.

Author's Contributions

KMN had substantially contributed to conception and design, data acquisition, interpretation and approval of the final draft. YA and MFK drafted the article and performed critical revision. All authors discussed the results and contributed to the final manuscript.

Financial Disclosures None

Conflict of Interests None

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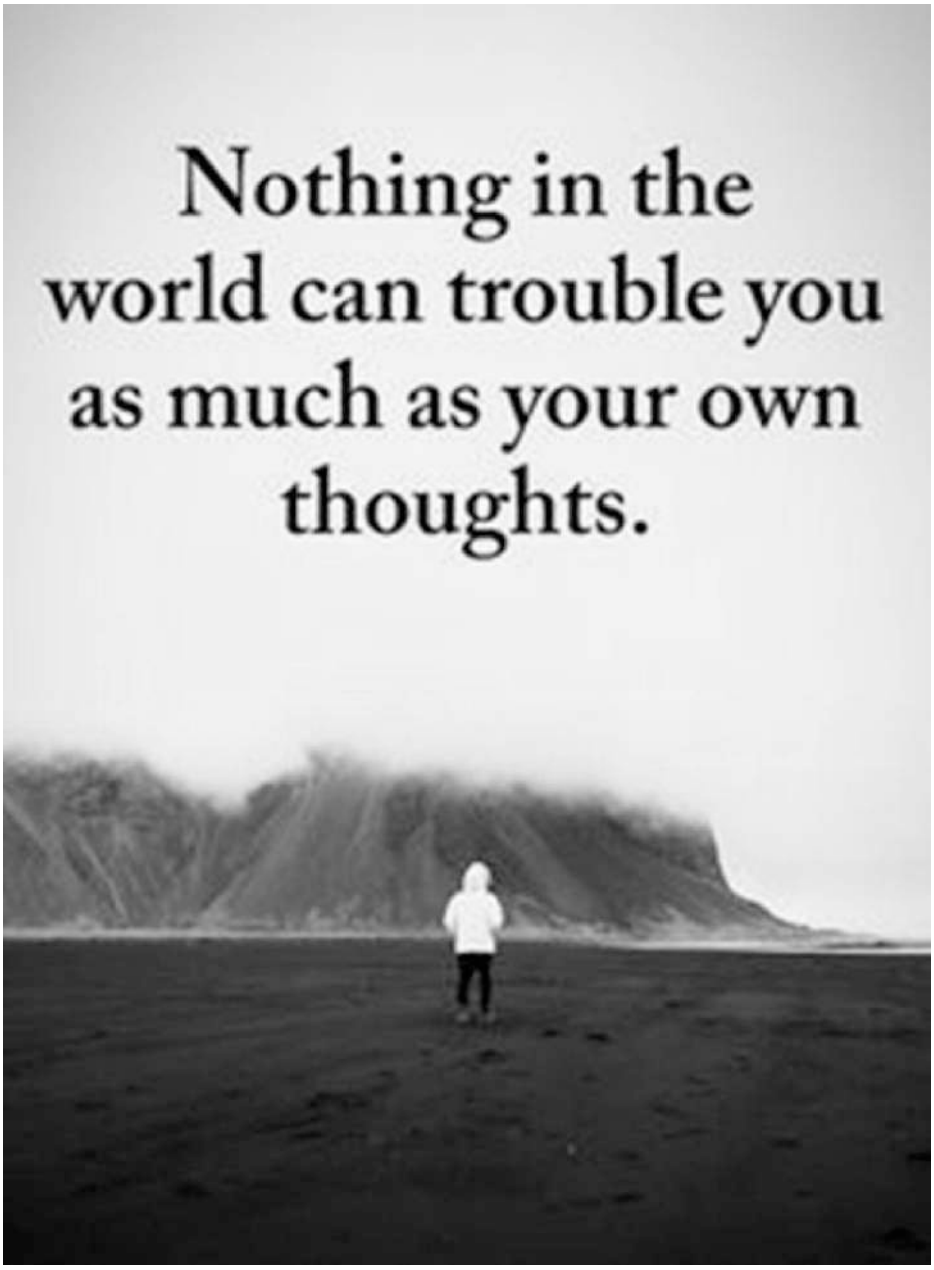

PROTECTIVE ROLE OF OCIMUM BASILICUM AGAINST ATROPHIC CHANGES INDUCED BY CYCLOPHOSPHAMIDE IN SECONDARY FOLLICLES OF ADULT FEMALE ALBINO RATS

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Abstract

Background: Cyclophosphamide is one of the alkylating chemotherapeutic drug used in cancer patients that has antifertility effects on female gonads. Ocimum Basilicum is a natural herb rich in polyphenols and is known to improve fertility.

Objective: The purpose of this study was to evaluate the role of natural herb, Ocimum basilicum extract, as a preventive agent against ovarian follicular toxicity induced by cyclophosphamide.

Methodology: 45 female albino rats were equally divided in control group A, experimental group B and group C each contained 15 rats. Group A rats received single dose of 150 mg/kg normal saline intraperitoneally on 8th day of experiment, while group B was given single intraperitoneal dose of 150 mg/kg cyclophosphamide at day 8 of experiment. Group C rats were pretreated with methanolic basil (Ocimum basilicum) seeds extract for 7 days followed by single intraperitoneal dose of 150 mg/kg cyclophosphamide at day 8 of experiment. All the rats were dissected 48 hours after the last dose.

Results: Secondary follicles were atrophied and showed atretic granulosa cells in group B when compared with control group A with p value <0.001. However, there was significant improvement in status of secondary follicles in group C, when compared with group B showing p value <0.025.

Conclusion: The present study depicts that basil seeds extract can prevent the cellular toxicity in secondary follicles caused by cyclophosphamide treatment. So the use of basil seeds during chemotherapy can significantly prevent its toxic effects on secondary follicles.

Key words: Cyclophosphamide, oxidative stress, follicular atrophy, basil.

Cyclophosphamide is a commonly used effective anticancerous alkaloid as well as an effective immunosuppressive drug. Cyclophosphamide showed the best desired result when tested against 33 tumours in comparison with 1000 other agents.[1] It is a useful alkylating drug that is a member of group oxazophosphorine and was first introduced by Bourseaux, Arnold and Brock in 1958.[2] This alkylating drug causes cytotoxicity by shifting its alkyl group to various constituents of tumour cells especially their DNA which causes cell death. Alkylation of guanine is very common and results in abnormal pairing of guanine and thymine resulting in formation of abnormal DNA strands.[3]

Cyclophosphamide is widely being used to treat malignant breast carcinoma, Hodgkin's lymphoma and autoimmune disorders like systemic lupus erythematosus and glomerulonephritis.[4,5,6] Cyclophosphamide, like other common chemotherapeutic drugs, has adverse effects on different organs of body. Severity of adverse effects has direct relation with the dose of drug. Most common side effects are immunosuppression, nausea, vomiting, myelosupp-

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ression, weight loss and loss of appetite.[7] It is known as a causative agent resulting in increased susceptibility to infections, haemorrhagic cystitis, nausea, vomiting, hair loss and secondary infertility in humans when given at therapeutic doses.[8]

Now a days, wide use of chemotherapeutic agents for treatment of lupus nephritis and breast carcinoma in young females is a big factor resulting premature menopause and secondary infertility due to ovarian failure.[9,10] The underlying mechanism of ovarian toxicity with cyclophosphamide is decreased levels of antioxidant enzymes i.e. superoxide dismutase and catalase, responsible for excess of free radicals resulting in oxidative tissue damage.[11] A study on female rats proved the dose dependent relationship between different doses of cyclophosphamide and antral follicular atresia.[12]

Basil plant is a member of family Lamiacaea, species Ocimum basilicum and Genus Ocimum.[13] Basil is known as "King of Herbs" due to its wide usage and advantages.[14] High content of phenolics compounds in extract of various parts of basil give it significant antioxidant potential in various in-vitro studies.[15] Basil has also been used along with other medicinal herbs for treatment of oligospermia in males, it resulted in significant improvement in levels of semen catalase and other sperm parameters proving that reduction in oxidative stress in gonads can improve chances of fertility because free radicles are known as a big factor in infertility.[16] An experiment on female rats also showed its strong antioxidant potential of its methanolic extract when given at dose of 1.5g/kg in combination with electromagnetic field (EMF) exposure and results showed significant improvement in various histological parameters of ovaries including granulosa cell apoptosis, fibrosis and venous congestion, when compared with the groups that received EMF exposure only.[17]

Cyclophosphamide is being frequently used during recent past years to treat malignancies. Major adverse effect of cyclophosphamide in young females having breast cancer, is secondary infertility as a result of its direct effects on primordial and growing follicles resulting in oxidative tissue damage.[18] It is clear from results of past studies that natural antioxidant agents show protective effects when used as a combination therapy with cyclophosphamide.[11] Present study is therefore done to check the antioxidant effect of basil seeds extract when given against cyclophosphamide induced toxicity in ovaries of adult female albino rats.

METHODOLOGY

This experimental study was performed in the Department of Anatomy, Shaikh Zayed Postgraduate Medical Institute, Lahore.

The sample size was estimated by using power and precision 3.0 software with 0.48 effect using and 2.28 as error SD. Based on this a total of 45 adult healthy female albino rats (3-4 months old), average female weight 190-240 gm were used in this study. All these animals were kept in cages in the animal house of the Department of Anatomy, Punjab PGMI, Lahore. The animals were allowed free access to food and water. A commercial brand of chick feed No. 1 was provided to rats, (Appendix-I). In every 5 kg of this feed, wheat flour 2.5 kg, molasses 1 kg, fish meal 100 grams and water was added. A 12:12 light: dark cycle was maintained. Temperature was maintained between 22-25 °C.

Basil seeds extraction was done with methanol. Nonvolatile compounds were extracted through solvent extraction method. Weighted samples were taken in a flask and then filled with solvent. These samples were then continuously shaken for 48 hours with 3 hours interval. Then the sample was filtered with filter paper and subjected to rotatory evaporation for removal of solvent and then through air evaporation. Sample was stored in freezer to avoid loss of antioxidant compounds.[19] Dosage solution for oral administration was prepared by dissolving extract in normal saline.[20] Cyclophosphamide was purchased from pharmacy and dose of drug as 150mg/kg body weight was calculated for each rat.

All rats were divided in three groups A, B and C. Each group contained 15 rats that were further

named as A1-A15, B1-B15 and C1-C15 by lottery method. The rats were assigned that number and marked with permanent marker and placed in the specific group cage. The weight of each rat was carefully recorded, with the help of weighing machine, in a proforma.

The dose schedule was as follows:

Group A (Control)

The rats of this group were not given any extract or toxic drug. These rats were provided with routine oral food daily and only given the single dose of normal saline 150 mg/kg body weight intraperitoneally on day 8 of experiment.20

Group B (Experimental)

The rats of this group received routine oral food with other rats for 7 days followed by only a single dose of 150 mg/kg cyclophosphamide intraperitoneally at day 8 of experiment.[b]

Group C (Experimental)

This experimental group received basil seed extract as dose of 1.5 g/kg/day through gastric intubation for 7 days followed by single 150 mg/kg intraperitoneal dose of cyclophosphamide at day 8 of experiment. The extract was given on the same fixed time daily.

All the animals of group A, B and C were properly given analgesia at the end of experiment, 48 hours after giving the last toxic dose, by using 50mg/kg ketamine followed by 50mg/kg xylazine intraperitoneally. The animals were dissected and ovaries were removed. Hematoxylin and eosin stained slides were prepared for both right and left ovaries of each rat having 5 serial tissue sections in each slide.

Graafian follicles were observed for atretic changes in their follicular cells. The follicle was considered tertiary when oocyte was seen surrounded by corona radiata cells and there was only a single large cavity between compacted layers of granulosa cells and corona radiata cells.[12] Granulosa cells were considered atretic when having pyknotic nuclei, irregular arrangement around oocyte and detachment from their basement membrane.[11]

Qualitative data for Graafian follicles was reported by using frequency and percentage for each group. Comparison was made among the groups by using Chi-square test. P value <0.05 was considered significant. Quantitative data was reported by using mean ± SD. Comparison among the groups was made by using ANOVA.

RESULTS

Secondary follicles were observed having normal shape and histology in all 15 rats of control group A, (fig. 1). Atresia was observed in 11 rats (73.3%) of toxic group B and only 4 rats (26.7%) of group C, (table 1).

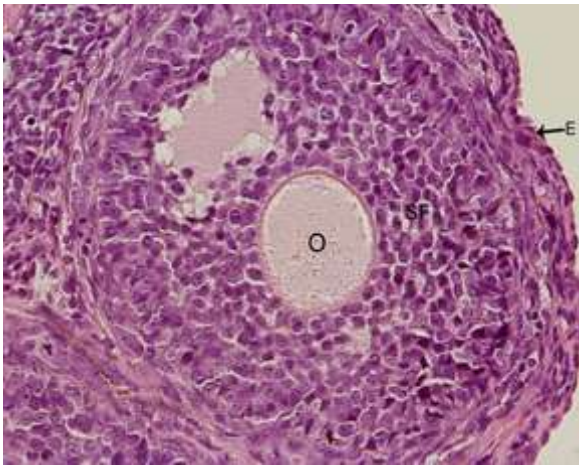

Figure1: *Photomicrograph of Secondary Follicle of Control Group A showing Normal Appearance (SF), Oocyte (O) and Epithelium (E), (H & E, 40x).*

Remaining rats in group B and C had normal and rounded secondary follicles having well defined arrangement of granulosa cells.

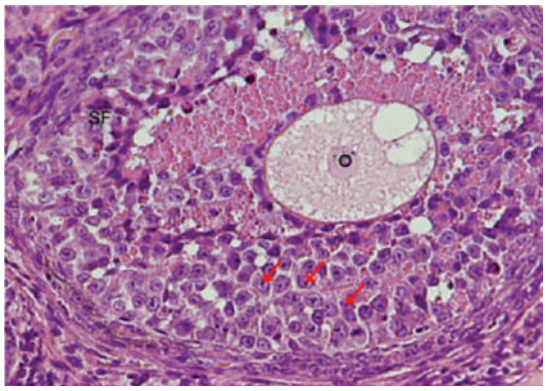

Figure2: *Photomicrograph of Rat Ovary of Experimental Group B having Atretic Changes in Secondary Follicle (SF) showing Pyknotic nuclei (red arrows) and Vacuolated Oocyte (O), (H & E, 40x).*

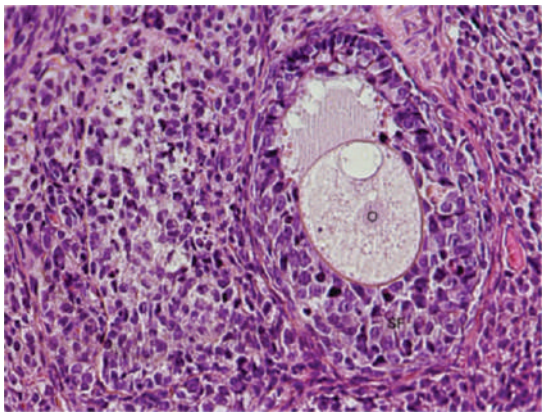

Figure 3: *Photomicrograph of Secondary Follicle of Experimental Group C Showing Secondary Follicle with Central Oocyte (O), (H & E, 40x).*

When group wise comparison was made between control group A and experimental group B, the results were highly significant with p-value <0.001. Comparison between experimental groups B and C showed improvement with p-value 0.011, (table. 2). The difference between control group and experimental group C still showed significant difference with p-value 0.013.

DISCUSSION

The follicles were labeled atretic because granulosa cells were pulled away from their basement membrane and from each other showing pyknotic nuclei. Granulosa cell layer was also irregular and with decreased thickness when compared with the secondary follicle of control group, (table 1, fig. 2, 3).

Table 1: *Group Wise Comparison for Status of Secondary Follicles between Control Group A, Experimental group B given Cyclophosphamide Alone and Group C given both Basil Extract and Cyclophosphamide.*

(I) Group	(J) Group	P-value
Group A	Group B	< 0.001**
	Group C	0.013*
Group B	Group C	0.011*

These changes observed in secondary follicles in toxic group B can be due to decreased levels of antioxidant enzymes and resulting overproduction of free radicles that caused toxic effects of cyclophosphamide resulting in initiation of cell damage followed by apoptosis of damaged cells.[11,21] Another mechanism that explains the cell death and apoptosis can be the cytotoxic action of phosphoramide mustard, one of the active metabolic compound of cyclophosphamide formed by liver.[22] This phosphoramide mustard caused alkylation of guanine base of DNA and resulted in formation of abnormal DNA in rapidly dividing cells causing cell cycle arrest and hence cell death followed by apoptosis in gonads.[3]

The significant improvement in status of secondary follicles was noted in group C, given basil seed extract and cyclophosphamide, (fig. 2, 3). This can be explained by the proved antioxidant and free radical scavenging potential of seed extract of Ocimum basilicum that can possibly be responsible for prevention of oxidative tissue damage in gonads of rats.[23-28] The antioxidant mechanism of action of Ocimum basilicum has also been proved in the study performed by Khaki A. In this study Ocimum basilicum extract protected the rat tissue against oxidative damage induced by electromagnetic field.[29]

CONCLUSION

The results of the present study proved that basil seed extract can prevent oxidative damage in secondary follicles when given as preventive agent along with cyclophosphamide by improving the atrophic changes in granulosa cells of secondary follicles induced by cyclophosphamide. The results also suggest the possible clinical use of basil seeds extract to prevent secondary infertility after cyclophosphamide treatment.

Limitation of Study

1) This study is duration is short due to limitation of time.
2) Due to limited resources and finances, this study is a preliminary study. More detailed studies can be performed in future.
3) It is an animal based study. Its results can be helpful for application of this concept in human beings.

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Conflicts of Interest

There was no conflict of interest.

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Contribution of Authors

The research was conducted by Dr. Saba Saleem. Dr. Sitwat Amna helped in statistical analysis of this research data. Dr. Kanwal Sharif did the proof reading of this article. The whole research was conducted under the supervision of Prof. Dr. Muhammad Suhail.

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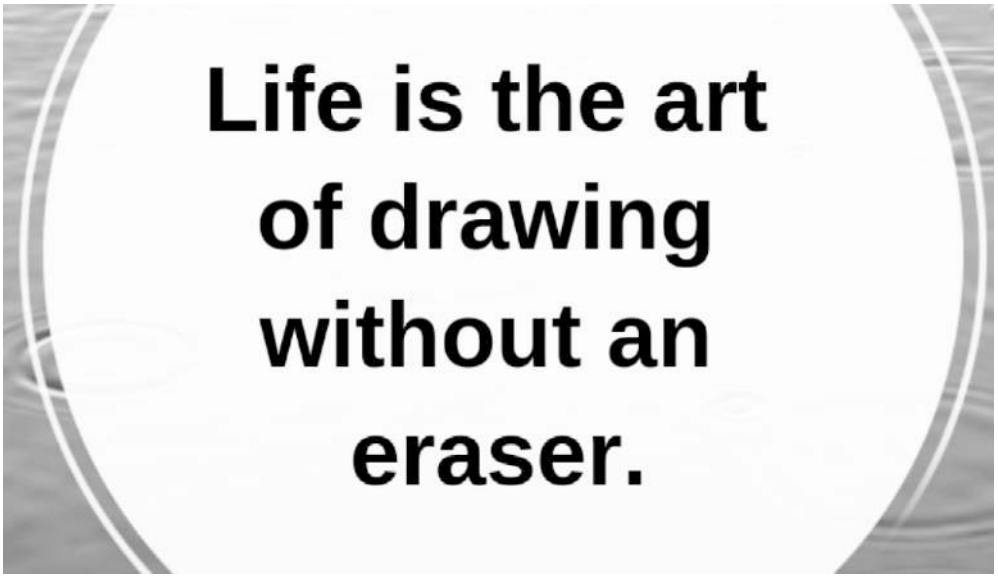

COMPARISON OF TOTAL INTRAVENOUS ANAESTHESIA (TIVA) WITH PROPOFOL AND ISOFLURANE ANAESTHESIA CAUSING CHANGE IN INTRAOCULAR PRESSURE OF PATIENTS UNDERGOING LAPAROSCOPIC CHOLECYSTECTOMY

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Abstract

Background: Physiological changes produced during laproscopic surgery lead to the increase in intraocular pressure (IOP). Anaesthetics agents including propofol and isoflurane are known to reduce the IOP.

Objective: To compare the mean changes in intraocular pressure of patients undergoing laparoscopic cholecystectomy, using total intravenous anaesthesia (TIVA) with propofol vs isoflurane anaesthesia.

Methodology: This randomized controlled trialwas carried out in the General surgery operation theatres of Mayo Hospital Lahore, Department of Anesthesiology from August 2016 to January 2017.60 adult patients fulfilling inclusion criteria were enrolled for the study. Patients were randomly allocated into two groups of 30 each. Patients in one group received total intravenous anaesthesia (TIVA) by infusion of propofol (Group A) while patients in the other group were maintained on isoflurane anaesthesia (Group B). IOP in both groups was measured after induction and after pneumoperitoneum.

Results: Baseline mean IOP was 17.17+0.95mmHg in P group and 17.70+1.39mmHg in S group (p value = 0.08).Final IOP was 13.93+1.19mmHg in P group and 15.10+1.37mmHg in S group, p value was 0.001 while mean change in IOP recorded was 3.27+0.83mmHg in P group and 2.53+0.51mmHg in S group with p value of 0.000 showing a statistically significant difference.

Conclusion: The mean change in intraocular pressure of patients undergoing laparoscopic cholecystectomy, using total intravenous anaesthesia (TIVA) with propofol is significantly lower when compared with isoflurane anaesthesia.

Key Words: Laparoscopic cholecystectomy, total intravenous anaesthesia (TIVA) with propofol, isoflurane anaesthesia, intraocular pressure (IOP)

Laparoscopic surgeries have the advantage of being minimally invasive and are associated with less postoperative pain and early mobilization of the patient.[1] Despite benefits, laparoscopic surgical techniques have a few distinct physiological and mechanical side effects. These include hypertension, increase in end-tidal CO_2 ($ETCO_2$.), increase in intra-abdominal, intra-ocular pressure (IOP) and central venous pressure (CVP).[2]

Hypoventilation, hypercapnia, increase in central venous pressure, lighter planes of anaesthesia, laryngoscopy and tracheal intubation, use of drugs like succinylcholine and ketamine and peribulbal block are all known to cause an increase in IOP during anaesthesia[3]. Changes in IOP are also associated with

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creation of pneumoperitoneum particularly with the patient placement in Trendelenburg position.[4] This increase in IOP may prove to be deleterious in susceptible patients.

Various techniques have been employed to counter the increase in IOP. These include laryngoscopy and intubation in deeper planes of anaesthesia, use of intravenous lidocaine before intubation, continuous infusions of propofol or thiopentone, hyperventilation during surgical procedure to reduce ETCO2 and gabapentin premedication.[5,6] Most induction agents and all volatile anaesthetics reduce IOP in proportion to the depth of anaesthesia. Propofol is known to decrease IOP by inhibiting somatodendritic AVP release from the supraoptic nucleus during surgery.[7] Previous studies have also shown decrease in IOP between 65% and 29% with propofol alone or in combination with remifentanil and succinylcholine.[8]

Isoflurane like most volatile anaesthetics reduces IOP by centrally mediated drop in systolic pressure, drop in CVP and reduction of aqueous humor production.[9] The overall result is a substantial control over IOP.

Agarwal M et al compared propofol infusion with isoflurane and studied their effect on IOP.[10] Patients were divided into two groups, both receiving propofol on induction along with atracurium. It was concluded in the study that on induction there was a similar decrease in IOP in all groups whereas 5 minutes after insufflation and 20° head down position IOP was significantly reduced in propofol infusion group (12.69±2.18, p=0.000. baseline at time of induction i.e. (17.27+1.87) and reduction in IOP was 4.58+0.31, p_0.537, 5 minute after pneumoperitoneum is established) as compared to decrease in isoflurane Group i.e. (2.9+1.17, p=0.798, baseline at time of induction 19.13+1.76 and 16.23+2.93 after induction in isoflurane group, p=0.000, 5 minute after pneumoperitoneum is established).

Sugata et al compared intraocular pressure changes using propofol and sevoflurane in prone spinal surgeries.[11] IOP values after positioning in the prone position were significantly higher than those at baseline in both groups (Propofol group: 8.9±3.5 to 13±1.5 mm Hg; Sevoflurane group: I1.6±3.9 to 13.2+0.5 mm Hg; PcO.OS). Although IOP values were higher in the sevoflurane group than in the propofol group, the differences in IOP values were not statistically significant. The results indicated that the choice of anesthetic agent, sevoflurane or propofol, did not have significant effects on IOP changes during a relatively short interval of prone spine surgery.

We have designed a study to evaluate the effects of propofol infusion compared to isoflurane on IOP during laparoscopic cholecystectomy to help us find an anaesthetic technique which may protect against increases in intraocular pressure during laparoscopic surgeries. This will rule out and evaluate the cause of discrepancy in literature about effect of propofol and isoflurane on reductions in IOP.

The aim of the study was tocompare the mean change in intraocular pressure of patients undergoing laparoscopic cholecystectomy, using total intravenous anaesthesia (TIVA) with propofol vs isoflurane anaesthesia.

METHODOLOGY

This randomized controlled trial was carried out in East and West operation theatres of Mayo Hospital Lahore at the Department of Anesthesiology from August, 2016 to January, 2017.After taking approval from Institutional Review Board of KEMU Lahore and RTMC CPSP, 60 adult patients fulfilling inclusion criteria were enrolled by expecting the mean change in intraocular pressure at T1 and T2 with Propofol and Isoflurane group as 4.58±0.31 and 2.9±1.17 respectively, by using 95% level of significance and 80 % power of study.[9] Patients with age 20-60 years of either sex, ASA class I or II, undergoing elective laparoscopic cholecystectomy for chronic cholelithiasis were included in the study, while the patients with history of ophthalmic disease e.g., glaucoma (>21 mmHg)(>126mg/dl), diabetic or hypertensive retinopathy, charact, patients on medications to lower I0P, with history of previous ocular surgery, patients who required rapid sequence

induction with succinylcholine (full stomach / gravid female) and those with anticipated difficult intubation were excluded.

Informed consent was taken from each patient. Brief history was taken and investigations (complete blood count, platelet count, clotting profile, renal and liver function tests) were reviewed. Patients were randomly allocated into two groups "group A" and "group B" of 30 each by using lottery method.

After shifting the patient to operating table, standard monitoring such as pulse oximeter, ECG and automatic non-invasive blood pressure (NIBP) was attached and base line readings were obtained. An intravenous line was secured and lactated Ringer's solution was started 4mL/kg/h.

Pre-oxygenation with 100% oxygen using bag mask was done for 3 minutes. In Group A induction was done with Inj. propofol 2-2.5 mg/kg and Inj. atracurium 0.5mg/kg. After bag mask ventilation for 3 minutes patient were intubated. A propofol infusion was started immediately after induction. Anaesthesia was maintained with propofol infusion (6-8 mg/kg /hr) with the help of infusion pump.

Pateints in Group Bwere also induced with Inj. Propofol 2-2.5 mg/kg and Inj. Atracurium 0.5mg/kg. Patientswere intubated after bag mask ventilation for 3 minutes. Isoflurane was started immediately after induction and anaesthesia was maintained with isoflurane at 1.3 MAC values via TEC 7 vaporizer. Patients with difficult intubation were excluded from the study. In both groups, oxygen in nitrous oxide (fraction of inspired oxygen 0.4) was administered using mechanical ventilation. Minute volume was adjusted to maintain an end tidal carbon dioxide concentration (ETCO2) between 32 and 38 mmHg throughout the procedure. A side-stream CO_2 monitor was used to measure ETCO.

Pneumoperitoneum was created by intraperitoneal insufflation of CO_2 with the patient in the Trendelenburg position. Throughout surgery, intra-peritoneal pressure was maintained at 13-15mmHg by a CO_2 insufflator. Intra-ocular pressure in both groups was noted using Schiotz tonometer. Measurements were taken (mean of 3 readings were taken)

- 5 minutes after induction in supine position, taken as baseline
- 5 minutes after pneumoperitoneum is established, in Trendelenburg position, taken as final outcome. Rest of the anesthesia was followed according to the patient and procedure need. Relevant demographic data like name, age and sex variables were recorded on the predesigned proforma.

The data analysis was done using statistical package for social sciences (SPSS) version 20. Age and intra-ocular pressure (baseline and final) and change in IOP were described as mean and standard deviation whereas gender was described as frequency and percentages. Independent sample T test was used to compare the mean IOP of Group A and Group B for significant difference. A p value of <0.05 was taken as significant.

RESULTS

Both groups A and B were comparable in terms of age, gender and ASA classification. (Table 1,2&3)

Mean IOP in group A was 17.17+0.95mmHg and in group B was 17.70+1.39mmHg at baseline with p value of 0.08, final IOP was 13.93+1.19 mmHg in A group and 15.10+1.37mmHg in group B (p value = 0.001) while mean change was recorded as 3.27+0.83mmHg in A group and 2.53+0.51mmHg in B group, p value was 0.000 showing a significant difference.(Table 4)

DISCUSSION

Laparoscopic cholecystectomy has numerous advantages, however, it is associated with an increase in intraperitoneal pressure and many other physiological changes that tend to increase intraocular pressure. Propofol total intra venous anaesthesia (TIVA) pre-

Table 1: Age Distribution

	Group	N	Mean age	Std. Deviation	Std. Error Mean	P value
AGE	GRP P	30	43.77	10.792	1.970	0.625
	GRP S	30	42.43	10.234	1.868	

Table 2: Gender Distribution (n=60)

Gender	Group-P (n=30)		Group-S (n=30)		
	No. of patients	%	No. of patients	%	p- value
Male	11	36.67	13	43.33	**0.598**
Female	19	63.33	17	56.67	
Total	**30**	**100**	**30**	**100**	

Table 3: Stratification with Regards to ASA Calss for Mean Change in IOP (n=60)

ASA class	Group-P (n=30)		Group-S (n=30)		P value
	Number of pts	frequency	Number of pts	frequency	
I	21	70%	17	56.66%	0.284
II	09	30%	13	43.33%	

Table 4: Comparison of Mean IOP (n=60)

IOP (mm Hg)	Group-P (n=30)		Group-S (n=30)		P value
	Mean	SD	Mean	SD	
Baseline	17.17	0.95	17.70	1.39	0.08
Final	13.93	1.19	15.10	1.37	0.001
Change	3.27	0.83	2.53	0.51	0.000

vents the increase in IOP with pneumoperitoneum (PNO) and head down position in laparoscopic surgeries. The mechanism of this propofol taming effect on IOP during laparoscopic surgery may be attributable to the effect of propofol on arginine vasopressin (AVP). Propofol inhibits the somatodendritic AVP release from the supraoptic nucleus and may therefore prevent the increase of IOP associated with PNO and the trendelenburg position.

This study was designed to evaluate the effects of propofol infusion compared to isoflurane on IOP during laparoscopic cholecystectomy to help us find an anaesthetic technique which may protect against increases in intraocular pressure during laparoscopic surgeries.

In our study, mean IOP was 17.17+0.95 mmHg in A group and 17.70+1.39 mmHg in B group was recorded at baseline, p value was 0.08, final IOP was 13.93+1.19mmHg in A group and 15.10+1.37 mmHg in group B, p value was 0.001 while mean change was recorded as 3.27+0.83mmHg in A group and 2.53+0.51mmHg in B group, p value was 0.000 showing a significant difference.

We compared our results with a previous study by Agarwal M et al who compared propofol infusion with isoflurane and studied their effect on IOP10. Patients were divided into two groups, both receiving propofol on induction along with atracurium. It was concluded in the study that on induction there was a similar decrease in IOP in all groups whereas 5 minutes after insufflation and 20° head down position IOP was significantly reduced in propofol infusion group (12.69±2.18, p=0.000. baseline at time of induction i.e. (17.27+1.87) and reduction in IOP was 4.58+0.31, p_0.537, 5 minute after pneumoperitoneum is established) as compared to decrease in isoflurane Group i.e. (2.9+1.17, p=0.798, baseline at time of induction 19.13+1.76 and 16.23+2.93 after induction in isoflurane group, p=0.000, 5 minute after pneumoperitoneum is established). The findings of our study are in agreement with the above study.

Another study by Sugata et al compared intraocular pressure changes using propofol and sevoflurane in prone spinal surgeries.[11] IOP values after positioning in the prone position were significantly higher than those at baseline in both groups (Propofol group: 8.9±3.5 to 13±1.5 mm Hg; Sevoflurane group: I1.6±3.9 to 13.2+0.5 mm Hg; PcO.OS). Although IOP values were higher in the sevoflurane group than in the propofol group, the differences in IOP values were not statistically significant. The results indicated that the choice of anesthetic agent, sevoflurane or propofol, did not have significant effects on IOP changes during a relatively short interval of prone spine surgery. Our findings are not supported by this study.

Agarwal[9] also reported that after induction with propofol IOP decreased by almost 50% while it decreased by almost 25% only after thiopentone induction. Mirakhur and Eti et al also reached the same conclusion when they measured IOP after propofol and thiopentone.[12,13]

Yamada et al observed the changes in IOP in dependant eye in lateral decubitus position. IOP significantly increased in both dependent and non-dependent eyes one hour after the patient was turned into lateral decubitus postion receiving sevoflurane anaesthesia

while no change was observed in the IOP of patients in propofol group.[14]

Muafi et al also compared the effect of propofol anaesthesia with isoflurane anaesthesia on IOP during laproscopic surgery concluding that propofol effectively prevents the increase in IOP in tredelenberg position.[15] With propofol TIVA the IOP increase was less as compared to isoflurane maintenance. This single observation endorses the hypothesis that the administration of propofol in any form (induction or TIVA) is better than isoflurane in controlling the rise in IOP. It was clarified that propofol induction and maintenance with propofol TIVA was the best option as regards the decrease in IOP as compared to isoflurane. Similar results were found by Lentschener et al., Demiroluk et al. and Vanacker et al. when they measured the effect of propofol on IOP used for induction and maintenance for anesthesia. They found that IOP was significantly below the baseline value and never exceeded the pre-induction value.[16-18]

In summary, we are of the view that "there is a difference in mean change in IOP from baseline pressure in isoflurane anesthesia versus propofol in patients undergoing laparoscopic cholecystectomy. However, someother multi center trials are required to validate our findings.

CONCLUSION

We concluded that the mean change in intraocular pressure of patients undergoing laparoscopic cholecystectomy, using total intravenous anaesthesia (TIVA) with propofol is significantly lower when compared with isoflurane anaesthesia.

Conflict of Interest None

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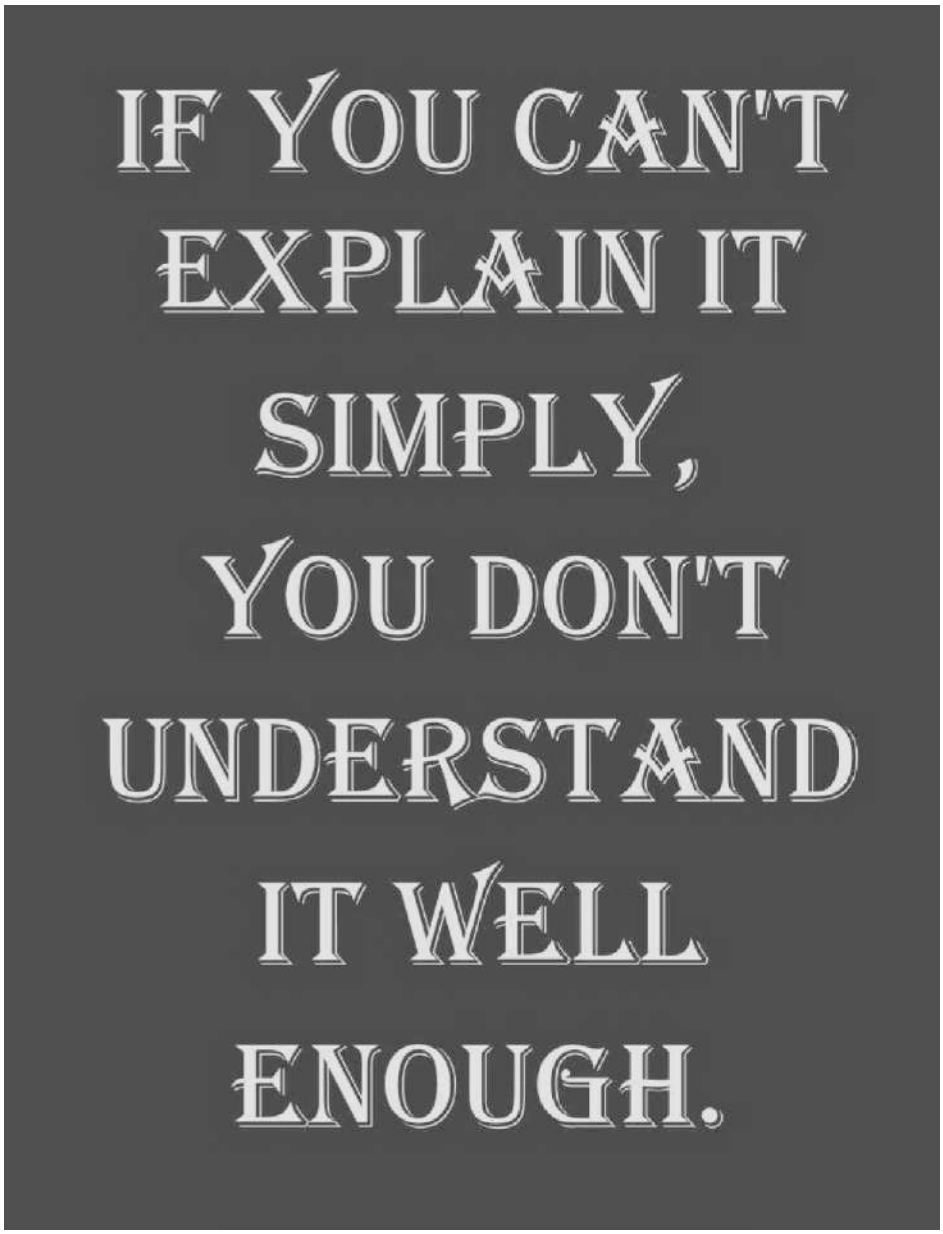

FREQUENCY OF DEPRESSION IN OPIOID ABUSERS

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Abstract

Background: Substance abuse is characterized by repeated acts of looking for the drug and using it, leading to dependency, increased tolerance level and decline in social and occupational functioning. Among many substances abused, the common ones are the opioids. Opioid abuse is frequently associated with psychiatric comor-bidities and one of the comorbidities, is depression.

Objective: To determine the frequency of depression in opioid abusers.

Methodology: A Cross sectional study was conducted in the Psychiatry Outpatient department of Sir Ganga Ram Hospital Lahore from April 2017 till October 2017. 246 patients were included in the study and were assessed using DAST-20 score to assess opioid abuse. Then HADS was applied to assess depression and its severity.

Results: Depression was present in 21.54% of the opioid abusers. Males were shown to have more depression i.e., 17.1% compared to females i.e., 4.5%. Middle aged patients had more depression i.e., 8.5%. Patients abusing opioids over short duration and belonging to lower socioeconomic status had higher rates of depression i.e., 11.8% and 14.2% respectively. Age was significantly associated with depression; rest of the effect modifiers had no association.

Conclusions: Opioid abusers have high rates of depression i.e., 21.54 %. Except age, no other effect modifier is associated significantly with depression.

Key Words: Opioids, depression, substance abuse

Substance abuse is characterized by repeated acts of looking for the drug and using it, leading to dependency, increased tolerance level and decline in social and occupational functioning.[1,2] Among many substances abused, the common ones are the opioids.[1,4] Opioids are substances that work by regulating opioid receptors throughout the body and produce morphine like effects. The worldwide prevalence of opioid abuse is around 0.6-0.8% in adult population[1].

Opioids are used for many purposes such as pain alleviation, controlling aggression and managing stress.[1,5] Opioids can be taken through various routes and depending on the route, these drugs have medical complications such as repeated infections, abscess formation, accidental overdose, and legal complication like involvement in criminal acts.[1]

In developed countries, the opioid drug most frequently associated with abuse and dependence is heroin; however, there is growing public health concern about prescription opioids, which are widely available, have significant abuse liability, and are used increasingly for purposes. Opioid addiction affects the young and the old, the wealthy and the poor, and the professional and the unemployed. Over the last few decades there have been significant advances in treatment and understanding of opioid dependence.

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It is increasingly accepted that opioid dependence is often a chronic, relapsing disorder amenable to medical treatment and intervention.[2]

Studies conducted in the past reveal that Opioid abuse is frequently associated with psychiatric comorbidities.[1,4,6] Among the comorbidities, the most commonly seen are depression (28%),[1,4] anxiety (29%)[4], personality disorder namely antisocial personality disorder (72%)[1] and borderline personality disorder (47%)[1], post-traumatic stress disorder (42%)[1] as well as dependency on other drugs[1]. About 15 percent of persons with opioid dependence attempt to commit suicide at least once.

Depression is characterized by low mood, decrease interest, fatigue, disturbed sleep, disturbed appetite, and depressive cognitions (hopelessness, helplessness, guilt, and ideas of self-harm), present most of the time every day for at least 2 weeks. It has been seen that opioid abusers have a high risk of developing depression.[1-8] The estimated prevalence of depression in opioid addicts is 20-28 %.[1,3,4]

In the Epidemiological Catchment Area (ECA) study, the lifetime history of substance use disorders, panic disorder, and OCD in major depression was approximately 27 percent, 10 percent, and 12 percent, respectively.[11,12] Comorbid substance use disorders and anxiety disorders worsen the prognosis of the illness and markedly increase the risk of suicide among patients who are suffering from major depression.

The factors contributing to the development of depression in opioid abusers are female gender, intravenous drug abuse, family conflicts and multiple previous failed attempts of quitting.[1]

Many international surveys have been conducted regarding the presence of depression comorbid with substance abuse. However, in Pakistan, no such study has been previously conducted. The aim of the current study was to determine the prevalence of depression in opioid abusers and to enhance the awareness among treating physicians to deal with this comorbidity that can be a hindrance in quitting opioid and thus interfering with patients social and occupational life. By promoting awareness, depression can be diagnosed efficiently, and early intervention can be done leading to reduce risk of relapse in opioid abusers.

METHODOLOGY

A cross sectional study was conducted at the outdoor of Psychiatry Department of Sir Ganga Ram Hospital Lahore from April 2017 till October 2017 after ethical approval. A total of 246 patients with opioid abuse were included in this survey after taking written consent, according to estimated 20% prevalence of depression in opioid abusers, with 5% margin of error and 95% confidence interval. Consecutive non-probability sampling technique was used to recruit participants between age 18-60 years with history of opioid use for over a year or more. Whereas previously diagnosed depressive patients or on antidepressant medication and abusing other substances were excluded.

Data about demographic profile (age, gender, socioeconomic status) and extent of opioid abuse was collected on a predesigned Performa and assessed by Drug Use Questionnaire (DAST-20 scale) for adults. Then HAD (Hospital Anxiety & Depression Scale) symptom checklist was applied to find the presence and severity of depression.

All the data were entered and analyzed using SPSS version 12.0. Quantitative data like age and HAD scores were presented by mean and standard deviation. Frequency and percentages were used for qualitative date like gender, depression, and severity of depression. Effect modifiers such as age, gender, duration of use, DAST-20 score (≥10, ≤10), and socioeconomic status were controlled through stratification. Post stratification chi square test was applied taking p value ≤0.05 as significant.

RESULTS

The mean age of the patients was 36.37 +9.816. The mean HADS score of the patients was 5.85 +3.78. Out of 246 patients, 80.49% were males and 19.51% were females. Depression was present in 21.54% of the patients (Table 1). Mild depression

was present in 9.76% of the patients, moderate depression in 7.72% and severe depression in 4.07% of the patients.

Data was stratified for age, gender, DAST-20 score, duration of use and socioeconomic status and chi square test was applied to see the association of depression with these effect modifiers. It was seen that only age was significantly associated with depression as show by the p value of 0.004 (Table 2). No other effect modifier was associated significantly with depression in opioid abusers.

Table 1: *Frequency of Depression in Patients with Opioid Abuse*

DEPRESSION	FREQUENCY	PERCENT
YES	53	21.54
NO	193	78.46
TOTAL	246	100.0

Table 2: *Frequency of Depression in Patients with Opioid Abuse*

AGE GROUPS	DEPRESSION		TOTAL	P-VALUE
	YES	NO		
YOUNG AGE (18-30 YEARS)	19 (7.7%)	37 (15.0%)	56 (22.8%)	0.004
MIDDLE AGE (31-50 YEARS)	21 (8.5%)	125 (50.8%)	146 (59.3%)	
OLD AGE (51-60 YEARS)	13 (5.3%)	31 (12.6%)	44 (17.9%)	
TOTAL	53 (21.5%)	193 (78.5%)	246 (100.0%)	

DISCUSSION

The aim of this study was to assess the frequency of depression among opioid abusers and the findings revealed that the level of depression inmiddle aged opioid abusers is significantly more as compared to other age groups.

A lot of research has been carried out internationally to assess the presence of depression in opioid abuse. A study conducted in South Africa by L Dannat in 2014 was based on assessing the frequency and contributing factors of comorbid psychiatric illness in patients with heroin use. The study assessed the participants for psychiatric illness, comorbid substance use and the legal and social complications associated with heroin use. The results showed that majority of the participants had been arrested due to involvement in drug related criminal activity and had disrupted family secondary to substance misuse. It was found that the most important psychiatric comorbidities were substance induced psychosis and major depressive disorder. Depression was higher in females and in those with alcohol use and intravenous drug use.[1]

Opioids are also used as analgesics and the analgesic effect also leads to dependence and increases the risk of mental health problems. Benedikt Fischer et al (2006), studied the association of depression with opioids that were used as an analgesic. The research concluded higher rates of comorbidity of both and reported that the mechanism involved includes the neurobiology and the impact of psychosocial factors.[7]

Similar results were reported by JF Scherrer et al in 2014, that depression was associated with opioids analgesics. They concluded that those participants who had been taking opioid analgesics for more than 90 days were more likely to develop depression compared to those with short duration of use.[8]

Another study was conducted by JF Scherrer in 2016, in which he again evaluated the prevalence of depression in patients using opioids as an analgesic. The results concluded that new onset depression after a use of opioid analgesic was present in around 12% of the patients in United States. The study evaluated the effect of two factors for an association with depression. One was the duration of opioid analgesic use and the other was the dose of the opioid as an analgesic medication. The study concluded that the longer the duration of opioid analgesic use the more are chances of developing new onset depression. However, the dose was not associated with depression.[9]

Patients suffering from non-cancer pain and using opioid analgesics are similarly associated with increased risk of recurrence of depression. This was

proved by one more study by JF Scherrer et al in 2016 in patients suffering from noncancerous pain. The study concluded that the rate of recurrence of dependence increases two folds if a patient is prescribed opioid analgesic compared to those who remain unexposed to opioids. The study revealed that the chances of recurrence are increased in those whose depression is already remitted.[10]

The associated of depression and its recurrence with opioids is well established. Another aspect of association of opioid with depression is its effect on the management of depression. This association was studied by JF Scherrer and its colleagues in 2016 and they concluded that longer term use of opioid analgesics was associated with development of treatment resistant depression.[11]

The current study has also revealed the association of depression with opioids abuse. However, the association of depression was only related to age and no other factors such as gender, duration of use and DAST-20 score had any effect on depression.

Our study had a few limitations such as cross-sectional design and being done at one center only, so the results could not be generalized. Also, it was conducted on a targeted population resulting in bias.

CONCLUSION

The current study concluded that depression is frequently present in opioid abusers. With higher frequency seen in males and those with lower social economic status, of middle age and with short duration. However, except age no other effect modifier was significantly associated with depression.

Limitations of study

- Our study being a cross sectional study has a limited value in a single hospital of a big city .we would also like to replicate the study in other cities to see if there are any differences in prevalence

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Authors Contributions

All six authors have contributed equally in conceptualization and detailed work of our project.

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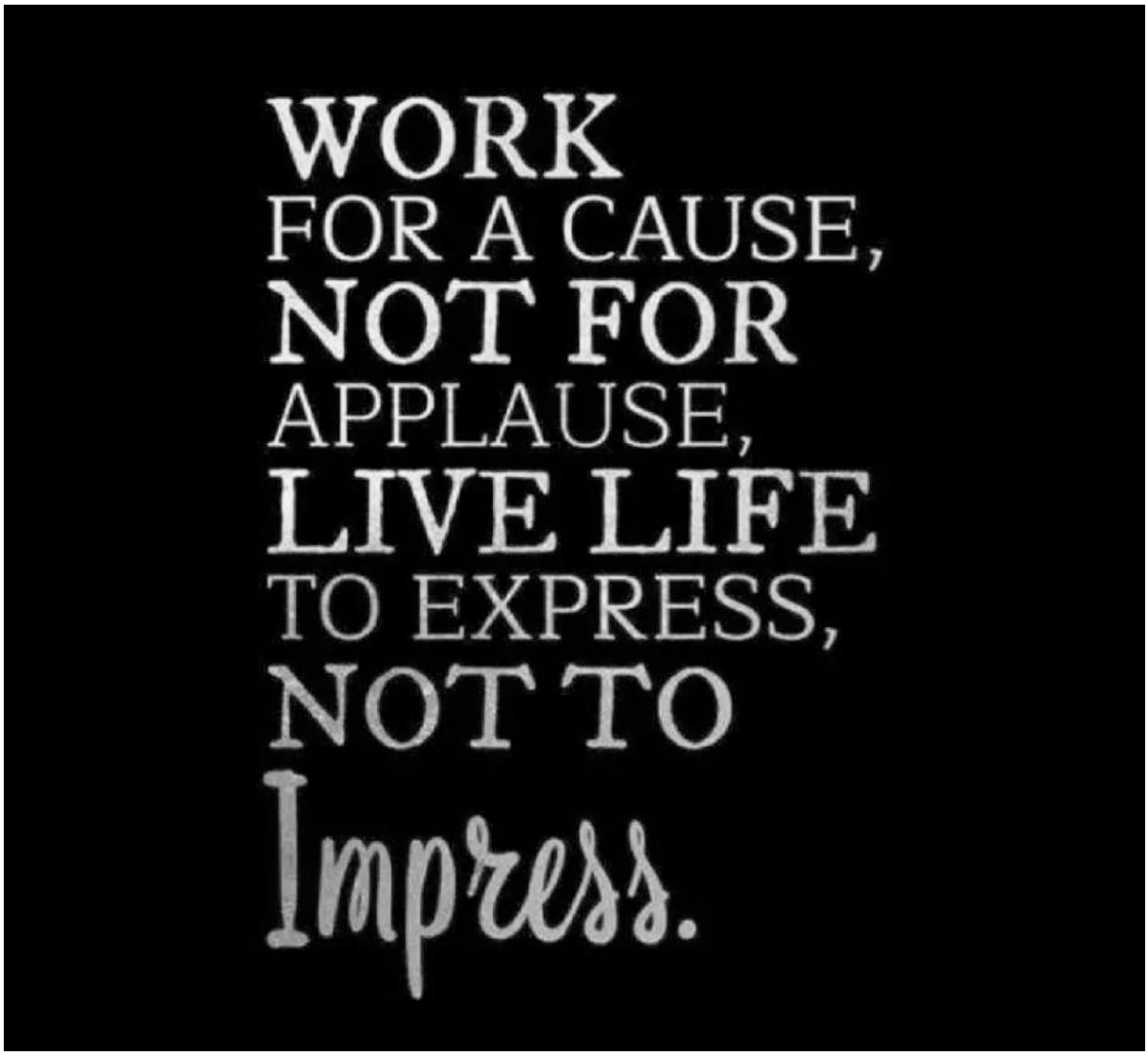

HISTOLOGICAL EVALUATION OF CERVICAL LYMPHADENOPATHY IN TERTIARY CARE HOSPITAL

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Abstract

Background: Cervical lymphadenopathy is a frequently encountered clinical entity. Etiology of cervical lymphadenopathy is diverse , ranging from non specific findings to malignant conditions. Proper investigations of palpable lymph nodes can lead to diagnosis of underlying serious medical conditions.

Objective: To determine prevalence rate of various etiologies of cervical lymphadenopathy.

Methodology: This is a retrospective study analysing various histological findings in 126 cervical lymph node biopsies presented in Akhter Saeed Medical and Dental College during JAN –DEC 2020.

Results: In this study, age range of the patients with cervical lymphadenopathy is 5-75 years. Male to female ratio is 1:1.5.The percentage distribution of cases in categories Reactive lymphoid follicular hyperplasia, Granulomatous lymphadenitis, Suppurative lymphadenitis, Kikuchi disease ,Non Hodgkin Lymphoma, Hodgkin Lymphomas and Metastatic are 58.7%(n=74), 23.8%(n=30),4.8%(n=6) , 0.8%(n=1),8%(n=10) ,2.3%(3)and 1.6%(n=2)respectively. Also, 88% cases are benign while 12% turned out to be malignant.

Conclusion: Most common cause of cervical lymphadenopathy in all age group is reactive follicular hyperplasia. However, among lymphomas, DLBCL is common in cervical lymphadenopathy.

Key words: Cervical, lymph nodes, histopathology

Lymph nodes are important component of lymphatic system, distributed in all over body. Lymphadenopathy is defined as variations in size (more than 1 cm), shape, or consistency of lymph nodes. It can be localised or generalised , acute or subacute.[1] Cervical region is considered as most common site for lymphadenopathy. Essential investigations, clinical, radiological and histological examination is crucial and can help in formulating accurate diagnosis of hidden diseases.[2] Differential diagnosis include nonspecific changes, infections, malignancies. Most common cause of infectious cause of lymphadenopathy in Pakistan is tuberculosis.[3]

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METHODOLOGY

Demographic data for all cervical lymph node biopsies was collected retrospectively from Akhter Saeed Medical and Dental College from 1st January 2020 to 30th December 2020. 126 patients were included in the study. The biopsies were routinely processed and stained by Haemotoxilin an Eosin stain and diagnosis of lymph nodes biopsies were made on histological examination and immunohistochemistry when needed. The data was analysed using SPSS Version 20.0 as frequency and percentages.

RESULTS

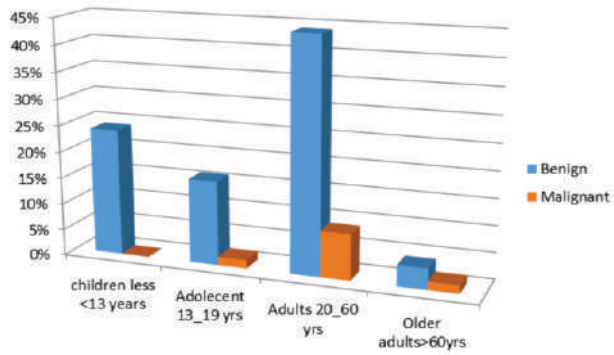
In the present study, age range of patients is 5-75 years, while Male to Female ratio is 1:1.5. Mean age is 32±13 years.

Table 1: *Pattern of Cervical Lymphadenopathy*

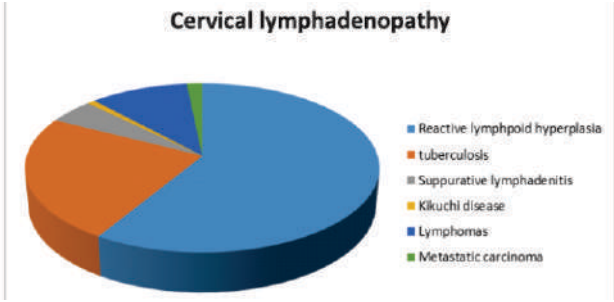
Histological Diagnosis	Number of patients	Percentage
Benign Lesions	**111**	**88%**
Reactive lymphoid follicular hyperplasia	74	58.7%
Tuberculous	30	23.8%
Suppurtive lymphadenitis	6	4.8%
Kikuchi disease	1	0.8%
Malignant Lesions	**15**	**12%**
Lymphoma		
Non Hodgkin lymphoma	10	8%
Hodgkin lymphoma	3	2.3%
Metastatic Carcinoma		
Squamous cell carcinoma	2	1.6%

Table 2: *Frequency of benign and malignant lesions of cervical lymph node in various age groups*

Age Group	No of patients (percentage)	Benign Cases (Percentage)	Malignant (Percentage)
Children < 13 years	30(24%)	30(24%)	0
Adolescent 13-19 years	22(17.5%)	20(16%)	2(1.6%)
Adults 20-60 years	67(53%)	56(44%)	11(8.7%)
Older adults > 60 years	07(5.5%)	5(4%)	2(1.6%)



Graph 1: *Distribution of Benign and Malignant Cases in different Age Groups*



Graph 2: *Various Histological Pattern of Cervical Lymphadenopathy*

In present study most of the cases were reactive follicular hyperplasia (58.7%), followed by tuberculous lymphadenitis (23.8%). Lymphoma represents (10.3 %) cases while metastatic turned out to be (1.6%).

DISCUSSION

Cervical lymphadenopathy is routinely observed by physicians in all age groups in Pakistan population. Lymph nodes can be enlarged due to nonspecific changes, infections or malignancies.[4] Incidence of tuberculous lymphadenitis in extrapulmonary tuberculosis in Pakistan population is almost 50 %, and more common in children and adolescent age group.[3] In malignant causes non Hodgkin lymphoma is predominant.[5] Thus, evaluation of cervical lymph node is crucial, as lack of proper investigations can miss diagnosis and can affect management of patients.

This study showed incidence of cervical lymphadenopathy is relatively more in males as compared to females .These findings are compareable with study done by Fazal-i-Wahid et al.[3]

Age is important predictor of diagnosis of benign versus malignant lymphadenopathy.[6] Our study also showed most of the cases in children and adolescent group are benign (96%) while frequency of malignant cases (10.3%) occur in adults and older adult groups is more than children and adolescent group (1.6%). Naseem et al also observed malignant cases are more common in second and third decade of life.[7] In contrast, Weinstock mentioned that most of the cases of cervical lymphadenopathy in children are caused by benign conditions.[8]

In this study benign cases are more common than malignant 88% vs 12 % (Table 1). In benign conditions reactive follicular hyperplasia and nonspecific changes predominate.[9] Also next to that, being most common infectious cause of cervical lymphadenopathy in Pakistan, Tuberculosis is really important to rule out in granulomatous lymphadenitis[10,11]. Similarly, majority of the cases in our study show features of reactive follicular hyperplasia (58.7%),

followed by granulomatous lymphadenitis most likely due to Tuberculosis(23.8%).

Malignancy is less common but serious cause of cervical lymphadenopathy.[12] The present study showed lymphoma turned out to be predominant in malignant category and 59% of the malignant cases proved to be DLBCL on immunohistochemistry Table #1. Deosthali in a systemic review on cervical lymphadenopathy also showed 46% of malignant cases proved to be Non Hodgkin lymphoma.[5]

CONCLUSION

Histological evaluation of cervical lymphadenopathy is vital, as early diagnosis of causative diseases has major impact on patient management .

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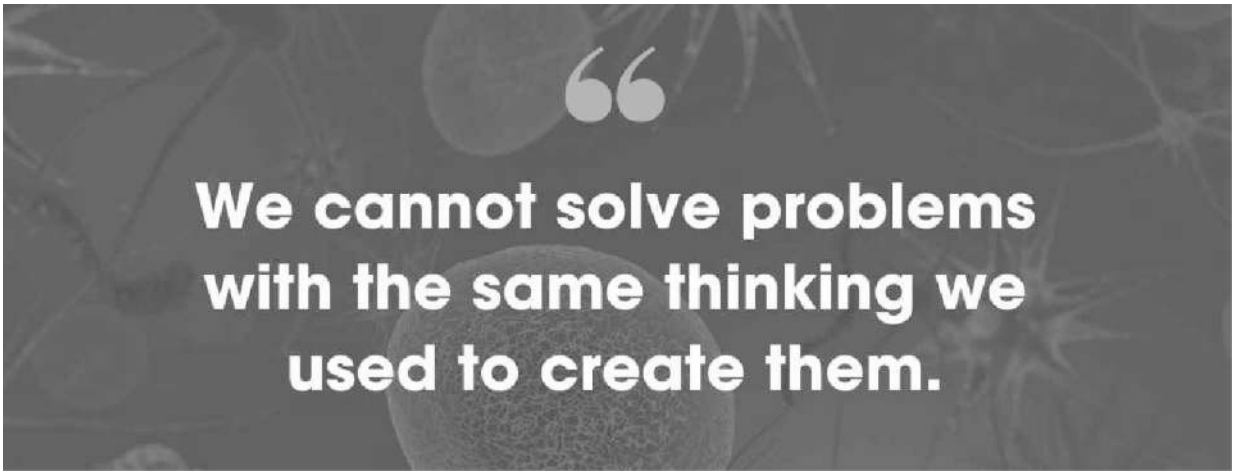

COMPLICATIONS OF TETANUS IN CHILDREN ADMITTED IN INTENSIVE CARE UNIT OF A TERTIARY CARE HOSPITAL

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Abstract

Background: Tetanus is often a fatal disease if left untreated. However, it is preventable by effective immunization. Patients with localized tetanus present with persistent rigidity in the muscle group close to the injury site. The diagnosis of tetanus is clinical with no particular laboratory test. Complications include spasm of the vocal cords and spasm of the respiratory muscles that cause interference with breathing. **Objectives:** Objective of study was to determine the frequency of complications of tetanus in children admitted in intensive care unit of a tertiary care hospital.

Methodology: It is a Descriptive case descriptive study, was conducted in Department of Intensive Care Unit, Children's Hospital & Institute of Child Health, Lahore during a period of 6 months from 13 March to 14 September 2020. By choosing Non- probability, consecutive sampling, Sample size of 95 children were calculated with 95% confidence level, 8.5% margin of error and taking expected percentage of respiratory tract infection i.e. 5% in children with tetanus. After meeting the inclusion criteria 95 children were enrolled. Patients were admitted in intensive care unit and were followed-up there. Patients were examined if they were developing respiratory infection, renal failure, sepsis, hypotension, need for mechanical ventilation. Then patients were followed-up in intensive care unit for 7 days. If patient were dead within hospital stay, then it was noted.

Results: In this study need of mechanical ventilation was observed in 67(70.5%) patients, respiratory tract infection was found in 32(33.7%) patients, hypotension was found in 60(63.2%) patients, renal failure was found in 37(38.9%) patients, sepsis was observed in 49(51.6%) patients and the mortality occurred in 14(14.74%) patients.

Conclusion: This study was concluded that the most common complication of tetanus was need of mechanical ventilation followed by hypotension and sepsis in children admitted in intensive care unit of a tertiary care hospital.

Key Words: Tetanus, Complications, Children, Intensive care unit

Tetanus is often a fatal disease if left untreated. However, it is preventable by effective immunization. Until now tetanus is still a threatening health problem in low- and middle-income developing countries. Globally reported deaths from tetanus in 2015 were 56,743.[1] There are complications of tetanus associated with tetanus illness and long-term critical care.[2,3] The existence and improvement of critical care facility provide a better tetanus management.[3]

Tetanus, a disease that is largely preventable, is still a major public health problem in the developing world and is associated with high morbidity and mortality rates. There is a paucity of published literature on tetanus.[4] The complications of tetanus result from muscle spasm, autonomic dysfunction, and

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prolonged critical illness. The mortality rate of tetanus is still high; it is because of various complications due to muscle spasms, autonomic dysfunction, as well as due to prolonged critical care. Management of tetanus with its complications is in intensive care facilities.[5] It has been reported that in 23 children with tetanus, following complications were reported to be high i.e. respiratory infection 21.7%, renal failure 65.2%, sepsis 43.5%, hypotension 73.9%, need for mechanical ventilation 65.2% and mortality 26.1%.[6] While another study found that in 44 children with tetanus, following complications were reported to be high i.e. need for mechanical ventilation 90% and mortality 18.18%.[7]

Rationale of this study is to determine the frequency of complications of tetanus in children admitted in intensive care unit of a tertiary care hospital. Literature has showed that there are very high chances of complications of tetanus in children admitted in a tertiary care hospital under treatment. But varied data has been retrieved from literature. Moreover, much work has not been done in this regard. So we want to conduct this study to confirm whether the complications are high or low. So that in future, we may plan a strategy to follow patients carefully and alter management protocols in order to decrease complications of tetanus. The Objective of study is to determine the frequency of complications of tetanus in children admitted in intensive care unit of a tertiary care hospital.

Tetanus: It was labeled if there was develop a reflex spasm of the masseters and bite the spatula by using spatula test,

Complications:

It was measured in terms of following:

1. Respiratory tract infection: presence of infection in lower respiratory tract including bronchi, bronchioles and lungs on chest x-ray with in 24 hour showing considerations.
2. Mechanical ventilation: if ventilator used to assist spontaneous breathing.
3. Hypotension: if blood pressure is less than 100/70mmg within 24 hours
4. Renal Failure: if creatinine>1.3mg/dl, eGFR< 90mL/min/1.73 m2 within 24 hours
5. Sepsis: if bacterial infection present in blood detected on blood culture with in 24 hour (105 organic 1+PF)
6. Mortality: if patient die within 7 days of hospital stay.

METHODOLOGY

It is a Descriptive case descriptive study, was conducted in Department of Intensive Care Unit, Children's Hospital & Institute of Child Health, Lahore during a period of 6 months from 13 March to 14 September 2020. By choosing Non- probability, consecutive sampling, Sample size of 95 children were calculated with 95% confidence level, 8.5% margin of error and taking expected percentage of respiratory tract infection i.e. 5% in children with tetanus. 95 children fulfilling the selection criteria were included in the study from emergency of Department of Pediatrics, The Children's Hospital & Institute of Child Health, Lahore. An informed consent was taken. Demographic informa-tion (name, age, gender, vaccination status, duration and cause of tetanus) was obtained. Then patients were admitted in intensive care unit and were followed-up there. Patients were examined if they were develop respiratory infection, renal failure, sepsis, hypotension, need for mechanical ventilation (as per operational definition). Then patients were followed-up in intensive care unit for 7 days. If patient were dead within hospital stay, then it was noted. All this information was noted on proforma. Data was entered & analysed by using SPSS version 21. Mean and standard deviation was calculated for quantitative variables like age and duration of tetanus. Qualitative variables like gender, cause of tetanus and complications (respiratory infection, renal failure, sepsis, hypotension, need for mechanical ventilation and mortality) was presented as frequency and percentage. Data was stratified for age, gender, socio-economic status, duration of symp-toms and

vaccination history to control effect modi-fiers. Post-stratification, chi-square test was done to compare complications in stratified groups. P-value ≤0.05 was considered a significant.

RESULTS

In this study total 95 patients were enrolled. The mean age of the patients was 8.43±3.56 years with minimum and maximum ages of 3 & 14 years respectively. According to this study there were 76(80.0%) patients were male and 19(20%) patients were females. Male to female ratio of the patients was 4:1.

In this study 52(54.74%) patients were belonged to low SES, 35(36.84%) belonged to middle and 8(8.42%) were belonged to high SES. Fig 2 Out of 95 patients, tetanus due to dental surgery was found in 3(3.16%) patients, tetanus due to injury on arm found in 5(5.26%) patients, tetanus due to injury on foot noted in 52(54.74%) patients, road side accident was 27(28.42%) patients, tetanus due to skull injury and tooth injury was found in 5(5.25%) and 3(3.16%) patients respectively.

The study results showed that the mean duration of symptoms of the patients was 7.59±3.06 weeks with minimum and maximum duration 2 & 12 weeks respectively. Table Of 95 patients, the vaccination status was noted in 24(25.3%) patients. Of 95 patients, mechanical ventilation was observed in 67(70.5%) patients, respiratory tract infection was found in 32(33.7%) patients, hypotension was found in 60(63.2%) patients, renal failure was found in 37(38.9%) patients and sepsis was observed in 49(51.6%) patients. Table In this study the mortality was occurred in 14(14.74%) patients.

In patients having age ≤ 8 years the mechanical ventilation was noted in 33(73.3%) patients while in patients having age >8 years the mechanical ventilation was noted in 34(68%) patients (p-value=0.569). In male patients the mechanical ventilation was noted in 55(72.4%) patients while in female patients the mechanical ventilation was noted in 12(63.2%) patients (p-value=0.431). In patients belonged to low SES the mechanical ventilation was noted in 37(71.2%) patients, in middle SES, the mechanical ventilation was noted in 23(65.7%) and in high SES patients the mechanical ventilation was noted in 7(87.5%) patients (p-value=0.721). Similarly insignificant difference was found between the mechanical ventilation and clinical variables. i.e. p-value>0.05.

In patients having age ≤ 8 years the respiratory tract infection was noted in 16(35.6%) patients while in patients having age >8 years the respiratory tract infection was noted in 16(32%) patients (p-value= 0.714). In male patients the respiratory tract infection was noted in 25(32.9%) patients while in female patients the respiratory tract infection was noted in 7(36.8%) patients (p-value=0.745). In patients belonged to low SES the respiratory tract infection was noted in 19(36.5%) patients, in middle SES, the respiratory tract infection was noted in 12(34.3%) and in high SES patients the respiratory tract infection was noted in 1(12.5%) patients (p-value=0.288). Similarly insignificant difference was found between the respiratory tract infection and clinical variables. i.e. p-value>0.05.

In patients having age ≤ 8 years the hypotension was noted in 27(60%) patients while in patients having age >8 years the hypotension was noted in 33(66%) patients (p-value=0.545). In male patients the hypotension was noted in 46(60.5%) patients while in female patients the hypotension was noted in 14(73.7%) patients (p-value = 0.288). In patients belonged to low SES the hypotension was noted in 34(65.4%) patients, in middle SES, the hypotension was noted in 19(54.3%) and in high SES patients the hypotension was noted in 7(87.5%) patients (p-value= 0.796). Similarly insignificant difference was found between the hypotension and clinical variables. i.e. p-value>0.05.

In patients having age ≤ 8 years the renal failure was noted in 20(44.4%) patients while in patients having age >8 years the renal failure was noted in 17(34%) patients (p-value=0.297). In male patients the renal failure was noted in 30(39.5%) patients while in female patients the renal failure was noted in 7(36.8%) patients (p-value=0.833). In patients belong-

ed to low SES the renal failure was noted in 21(40.4 %) patients, in middle SES, the renal failure was noted in 12(34.3%) and in high SES patients the renal failure was noted in 4(50%) patients (p-value= 0.965). Similarly insignificant difference was found between the renal failure and clinical variables. i.e. p-value >0.05.

In patients having age ≤ 8 years the sepsis was noted in 23(51.1%) patients while in patients having age >8 years the sepsis was noted in 26(52%) patients (p-value=0.931). In male patients the sepsis was noted in 41(63.9%) patients while in female patients the sepsis was noted in 8(42.1%) patients (p-value=0.356). In patients belonged to low SES the sepsis was noted in 28(53.8%) patients, in middle SES, the sepsis was noted in 16(45.7%) and in high SES patients the sepsis was noted in 5(62.5%) patients (p-value=0.923). Similarly insignificant difference was found between the sepsis and clinical variables. i.e. p-value>0.05.

In patients having age ≤ 8 years the mortality was noted in 7(15.6%) patients while in patients having age >8 years the mortality was noted in 7(14%) patients (p-value=0.831). In male patients the mortality was noted in 13(17.1%) patients while in female patients the mortality was noted in 1(5.3%) patients (p-value=0.288). In patients belonged to low SES the mortality was noted in 9(17.3%) patients, in middle SES, the mortality was noted in 05(14.3%) and in high SES patients the mortality was noted in 0(0.0%) patients (p-value=0.262). Similarly insignificant difference was found between the mortality and clinical variables. i.e. p-value>0.05.

DISCUSSION

Tetanus is an acute infectious disease caused by the bacterium, Clostridium tetani ©. tetani), as defined by the World Health Organization,[8] which generates a neurologic toxin[16] Because of the high mortality rate, tetanus is still a significant issue worldwide, especially in developing counties. Since Pakistan is an agricultural state and the disease is common where soil is cultivated, in rural areas, warm climates and among males, so being a tetanus prone country, vaccination against tetanus is imperative for our children. Tetanus often leads to death, with a reported 213, 000–293,000 deaths worldwide.[9]

In this study mean age of the patients was 8.43±3.56 years, there were 76(80.0%) patients were male and 19(20%) patients were females. A study by Zhe Fan et al[10] presented in their study that the percentage of males (70.6%) was greater than the percentage of females (29.4%). Fawibe[11] reported 85.7% males and 14.3% females and Chukwubike and God's power[12] reported 58.1% males and 41.9% females in their studies. Lau LG et al showed in their study that male predominance was seen in post trauma cases (7 out of 9, 77.77%), because the boys are more involved in outdoor activities as compared to girls.[9] Mondkar et al[13] showed in their study the mean age 6.6 years. Out of 25 patients 16 were males and 9 were females. Males often do outdoor jobs, such as farming or skilled jobs that have an increased probability of injuries. In our study the most common cause of injury was due to foot injury noted in 52(54.74%) patients followed by road side accident, skull injury and injury on arm respectively. Different studies showed that Regarding the site of trauma, majority (6 out of 9, 66.66%) had injury to lower limbs (toe, sole, shin) which is also supported by other studies.[14] One of our patient

Frequency Distribution of Vaccination Status

		Frequency	Percent
Vaccination status	Yes	24	25.3
	No	71	74.7
	Total	95	100.0

Frequency Distribution of Complications

		Frequency	Percent
Mechanical Ventilation	Yes	67	70.5
	No	28	29.5
Respiratory tract infection	Yes	32	33.7
	No	63	66.3
Hypotension	Yes	60	63.2
	No	35	36.8
Renal Failure	Yes	37	38.9
	No	58	61.1
Sepsis	Yes	49	51.6
	No	46	48.4

Comparison of Mechanical Ventilation between Clinical and Demographic Variables

		Mechanical Ventilation		Total	p-value
		Yes	No		
Age	⩽ 8	33	12	45	0.569
		73.3%	26.7%	100.0%	
	>8	34	16	50	
		68.0%	32.0%	100.0%	
Gender	Male	55	21	76	0.431
		72.4%	27.6%	100.0%	
	Female	12	7	19	
		63.2%	36.8%	100.0%	
SES	Low	37	15	52	0.721
		71.2%	28.8%	100.0%	
	Middle	23	12	35	
		65.7%	34.3%	100.0%	
	High	7	1	8	
		87.5%	12.5%	100.0%	
Duration of symptoms	⩽6	26	7	33	0.198
		78.8%	21.2%	100.0%	
	>6	41	21	62	
		66.1%	33.9%	100.0%	
Cause of injury	Injury on foot	39	13	52	0.293
		75.0%	25.0%	100.0%	
	Other injuries	28	15	43	
		65.1%	34.9%	100.0%	
Vaccination	Yes	17	7	24	0.970
		70.8%	29.2%	100.0%	
	No	50	21	71	
		70.4%	29.6%	100.0%	

Comparison of Sepsis between Clinical and Demographic Variables

		Sepsis		Total	p-value
		Yes	No		
Age	⩽ 8	23	22	45	0.931
		51.1%	48.9%	100.0%	
	>8	26	24	50	
		52.0%	48.0%	100.0%	
Gender	Male	41	35	76	0.356
		53.9%	46.1%	100.0%	
	Female	8	11	19	
		42.1%	57.9%	100.0%	
SES	Low	28	24	52	0.923
		53.8%	46.2%	100.0%	
	Middle	16	19	35	
		45.7%	54.3%	100.0%	
	High	5	3	8	
		62.5%	37.5%	100.0%	
Duration of symptoms	⩽6	17	16	33	0.993
		51.5%	48.5%	100.0%	
	>6	32	30	62	
		51.6%	48.4%	100.0%	
Cause of injury	Injury on foot	30	22	52	0.190
		57.7%	42.3%	100.0%	
	Other injuries	19	24	43	
		44.2%	55.8%	100.0%	
Vaccination	Yes	14	10	24	0.444
		58.3%	41.7%	100.0%	
	No	35	36	71	
		49.3%	50.7%	100.0%	

developed tetanus after dog bite.[8]

In this study mechanical ventilation complication was observed in 67(70.5%) patients, respiratory tract infection was found in 32(33.7%) patients, hypotension was found in 60(63.2%) patients, renal failure was found in 37(38.9%) patients and sepsis was observed in 49(51.6%) patients and mortality occurred in 14(14.74%) patients. Some of the studies are discussed below showing their results as.

Naseem et al.,[6] reported that in 23 children with tetanus, following complications were reported to be high i.e. respiratory infection 21.7%, renal failure 65.2%, sepsis 43.5%, hypotension 73.9%, need for mechanical ventilation 65.2% and mortality 26.1%.[6] Regarding the outcome, tetanus has a mortality rate ranging between 20 to over 50% as mentioned in various studies.[15] One study by Mondkar et al.,[13] documented in their study that in tetanus patients the complications encountered were pneumonia (58%), conjunctivitis (41%), gastrointestinal bleed (37.5%), urinary infection (33%), acute kidney injury (AKI) following rhabdomyolysis (33%), sepsis (29%), disseminated intravascular coagulation (DIC) (25%), bedsores (25%), and acute respiratory distress syndrome (ARDS) (20%). Oral diazepam was most commonly used, followed by midazolam, vecuronium, and magnesium sulfate. Mortality rate was 32% (five moderate and three severe cases died). Another study found that in 44 children with tetanus, following complications were reported to be high i.e. need for mechanical ventilation 90% and mortality 18.18%.[7]

Duggal et al., resulted in their study that the mortality rate 16(21.6%) was significantly associated with shorter duration of stay ($p<0.001$). Mortality was high among unvaccinated children compared to

vaccinated children (p=0.01). Vaccination coverage was found to be inadequate and post-trauma immune prophylaxis had been ignored. Suresh Kumar Angurana et al[18] presented patients with higher mortality rate as compared to our study. The author reported mortality rate (40%) within the range reported by other studies from developing countries (4.1–78.9%)[25] Angurana et al.,[28] showed the common complications noted were respiratory failure, rhabdomyolysis, AKI, autonomic dysfunction (in second week of illness) and HCAIs. Rhabdomyolysis in tetanus is due to generalized muscle spasms. Myoglobinuria, hypo-ten-sion, diazepam and sepsis can lead to AKI.[29]

CONCLUSION

This study was concluded that the most common of tetanus was need of mechanical ventilation followed by hypotension and sepsis in children admitted in intensive care unit of a tertiary care hospital, moreover we came to know from this study that the vaccination status was very poor among children.

Limitations of Study It is among the few studies in our setup about the complications of Tetanus in children's admitted in Intensive care units. Limitation of study is that its results can't be generalized over large geographic area because its data is collected from one Tertiary care hospital.

Ethical Approval This study was approved by Ethical Review Committee of The Children's Hospital, Lahore. Vide reference No. 1/131/20 dated October 22, 2020.

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Conflict of Interests There is no conflict of interests with other studies.

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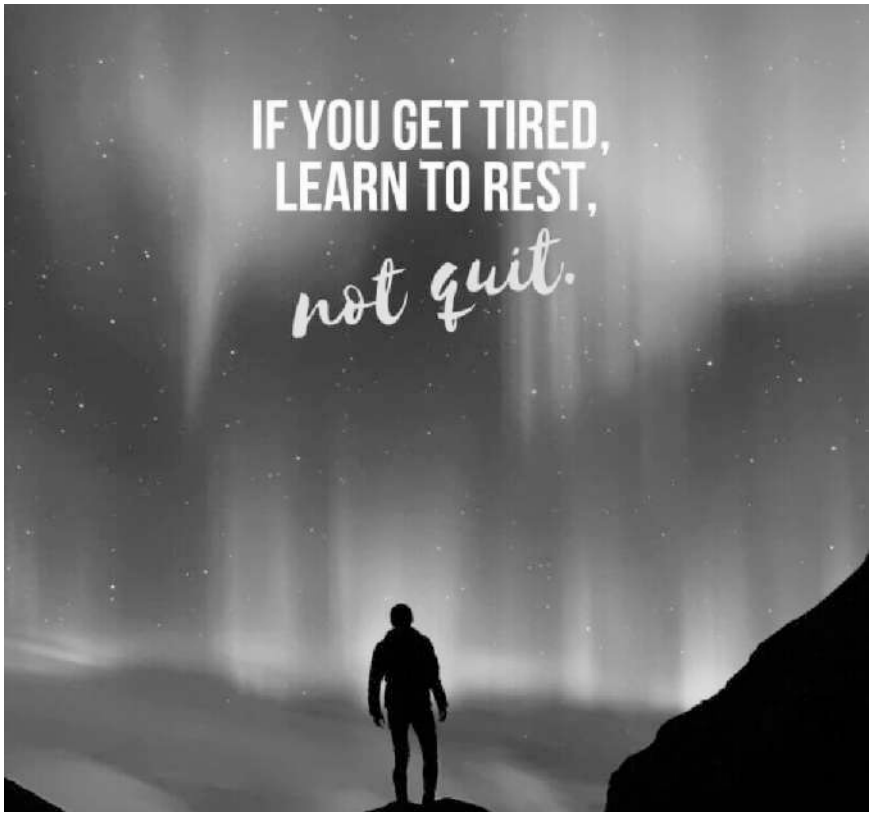

DIAGNOSTIC ACCURACY OF HIGH-RESOLUTION COMPUTED TOMOGRAPHY IN DIAGNOSING CHOLESTEATOMA, TAKING HISTOPATHOLOGY AS GOLD STANDARD

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Abstract

Objectives: To determine the diagnostic accuracy of high-resolution computed tomography in diagnosing cholesteatoma, taking histopathology as gold standard. It was a descriptive, cross-sectional. Study Duration was July 2020 to December 2020, in the Department of Radiology, Jinnah Hospital / Allama Iqbal Medical College, Lahore.

Methodology: A total of 130 patients having clinically suspected cholesteatoma of age 12-50 years and both genders were included. Patients with previous history of middle ear surgery and history of trauma to ear were excluded. High resolution CT scan of temporal bone was performed in all the patients and presence or absence of cholesteatoma was noted. HRCT scan findings were compared with histopathology findings.

Results: Mean age was 27.72 ± 10.24 years. Out of these 130 patients, 73 (56.15%) were males and 57 (43.85%) were females with ratio of 1.3:1. In HRCT positive patients, 69 (True Positive) had cholesteatoma and 04 (False Positive) had no cholesteatoma on histopathology. Among 57, HRCT negative patients, 05 (False Negative) had cholesteatoma on histopathology whereas 52 (True Negative) had no cholesteatoma on histopathology (p=0.0001). Overall sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of high resolution computed tomography in diagnosing cholesteatoma, taking histopathology as gold standard was 93.24%, 92.86%, 94.52%, 91.23% and 93.08% respectively.

Conclusion: This study concluded that diagnostic accuracy of high resolution computed tomography (HRCT) in diagnosing cholesteatoma is quite high.

Key Words: cholesteatoma, computed tomography.

Cholesteatoma is an aggressive temporal bone mass composed of keratinizing stratified squamous epithelium. Acquired middle ear cholesteatoma, which is more common than congenital variety has been recognized clinically and radiologically for many years.[1,20,21] Cholesteatoma is potentially serious condition as it can progressively enlarge and erode into neighbouring structures, giving rise to serious intracranial and extracranial complications. Cholesteatoma can be recognized by the presence of attic squames on otoscopic examination.[2] The clinical manifestations of cholesteatoma are quite variable, ranging from an asymptomatic phase to life-threatening complications.[3] The diagnosis of middle ear cholesteatoma can be made simply by an otoscopic examination, in addition to endoscopic and microscopic evaluation or even surgical exploration. In a study, prevalence of cholesteatoma was found to be 61.0%.[4]

Many imaging modalities are available for the evaluation of the temporal bone, including plain radiographs, contrast cisternography, computed tomography (CT), and magnetic resonance imaging (MRI).[5] CT scanning is the imaging modality of choice in the

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diagnosis of cholesteatomas because it can detect subtle bony defects. However, CT scanning cannot always distinguish between granulation tissue and a cholesteatoma. Even technically excellent fine-cut CT scans cannot reliably determine the full extent of disease. With the introduction of modern HRCT scanners, it has been made possible to identify many important structures not previously demonstrated by X-ray radiography. HRCT has thus transformed temporal bone imaging and has substituted the earlier modalities.

The advent of HRCT has made a significant impact on the surgical management of individuals with middle ear disease. It confirms and expands upon the otoscopic findings, resolves clinical doubts, and in many circumstances plays a significant role in determining surgical technique when surgery is necessary. The surgical approach can be planned on the basis of HRCT findings.[6,7,22] High-resolution computed tomography (HRCT) offers excellent spatial and density resolution using special algorithms. It provides information not only about bony outline but also soft tissue changes making it possible to demonstrate the location and extent of disease as well as its complications.[8,20]

One study has shown the sensitivity and specificity of high resolution computed tomography in diagnosing cholesteatoma as 89.29% and 77.22% respectively.[9] In a study of 64 patients with middle ear cholesteatomas, Gaurano and Joharjy found that the diagnosis of these cholesteatomas was suggested by specific characteristics found on CT scans. These included expansion of the aditus and mastoid antrum (92% of patients) and ossicle erosion (also 92% of patients). Preoperative CT scans in the study had 97% correlation with surgical and histopathologic findings.[10]

Cholesteatoma extension is the most important factor affecting the outcome of the patients, and has an important bearing on planning treatment, so its pre-operative evaluation by non-invasive imaging modality has utmost importance in planning the treatment. The rationale of this study was to determine the diagnostic accuracy of high resolution computed tomography in diagnosing cholesteatoma, taking histopathology as gold standard. This study will be a useful addition in the existing literature and our population will also be provided with a noninvasive and easily available imaging modality for pre-operative assessment of cholesteatoma which will further help the surgeons for selection of proper surgical approach in order to reduce the morbidity of these particular patients.

METHODOLOGY

It was a Descriptive, cross-sectional study in the Department of Radiology, Jinnah Hospital / Allama Iqbal Medical College, Lahore from July 2020 to December 2020. Sample size of 130 cases has been calculated with 95% confidence level, preva-lence of cholesteatoma as 61.0%4, 6% desired prec-ision for sensitivity of 89.29% and 10% desired preci-sion for specificity of 77.22% of HRCT in diagnosing cholesteatoma.[9] It was a non-probability, consecutive sampling. Inclusion Criteria: All patients having clinically suspected cholesteatoma (as per-operational definition) of >3 months' duration. Patients 12-50 years of either gender. Exclusion Criteria: Patients with previous history of middle ear surgery. Patients with history of trauma to ear. Patients not willing for surgery.

Total number of 130 patients who were referred to the Radiology Department of Jinnah Hospital / Allama Iqbal Medical College, Lahore, fulfilling the inclusion criteria was selected. Informed written consent was taken from each patient. High resolution CT scan of temporal bone was performed in all the patients. CT protocol included CT with axial slices. The CT scan findings were interpreted by one consultant radiologist (with at least 5 years of post-fellowship experience) and presence or absence of cholesteatoma was noted. All the patients underwent surgery and the resected specimen was sent to the institutional laboratory and report was interpreted by the consultant histopathologist (with at least 5 years of post-fellowship experience) and presence or absence of cholesteatoma was noted. HRCT scan findings were com-

pared with histopathology findings. This all data including the demographic data was recorded on a specially designed proforma.

Collected data was analyzed through computer software SPSS 22. Age and duration of disease were presented as mean and standard deviation. Gender and cholesteatoma (present/absent) on HRCT and histopathology were presented as frequency and percentage. Data was used to calculate the sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of high resolution computed tomography (MDCT) in diagnosing cholesteatoma.

RESULTS

Age range in this study was from 12-50 years with mean age of 27.72 ± 10.24 years. Majority of the patients 31.54% were between 12-20 years of age.

Out of these 130 patients, 73 (56.15%) were males and 57 (43.85%) were females with ratio of 1.3:1. Mean duration of disease was 7.87 ± 5.34 months.

All the patients were subjected to high resolution computed tomography scanning of temporal bone and HRCT scan supported the diagnosis of cholesteatoma in 73 (56.15%) patients and no cholesteatoma in 57 (43.85%) patients. Histopathology findings confirmed cholesteatoma in 74(56.92%) patients and no cholesteatoma in 56(43.08%) patients. In HRCT positive patients, 69(True Positive) had cholesteatoma and 04 (False Positive) had no cholesteatoma on histopathology. Among 57, HRCT negative patients, 05 (False Negative) had cholesteatoma on histopathology whereas 52 (True Negative) had no cholesteatoma on histopathology (p=0.0001) as shown in Table I

Overall sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of high resolution computed tomography in diagnosing cholesteatoma, taking histopathology as gold standard was 93.24%, 92.86%, 94.52%, 91.23% and 93.08% respectively (Fig. 1)

DISCUSSION

A major advance in diagnostic imaging has occurred with the introduction of High Resolution computed Tomography which have made it possible to obtain high quality images with exquisite demonstration of most normal temporal bone structures and numerous pathological processes. High resolution computed tomography provides excellent of bony land marks within the temporal bone, due to the temporal bone inherent contrast, its dense bone being surrounded by air of the tympanic cavity and mastoid air cells. It has also added whole new dimension to the temporal bone by allowing visualization of the of the tissue components within and adjacent to the temporal bone. Because high resolution computed tomography can assess this area with unprecedented accuracy, it has allowed better understanding of the etiology, pathology, the disease course earlier detection of complications and treatment modality which has considerably reduced the morbidity and mortality pertaining to lesions.[11]

Table 1: *HRCT and Histopathology Findings*

	Positive result on Histopathology	Negative result on Histopathology	P-value
Positive result on HRCT	69 **(TP)***	04 **(FP)*****	**0.0001**
Negative result on HRCT	05 **(FN)****	52 **(TN)********	

*-TP=True positive **-FP=False positive
-FN=False negative *-TN=True negative

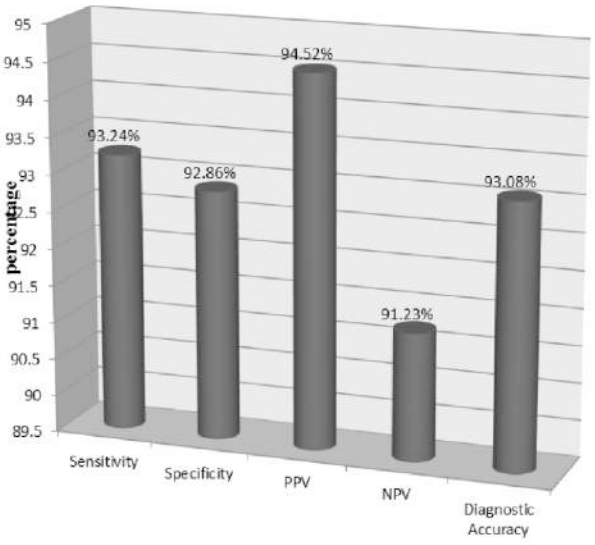

Figure-1: *Diagnostic Accuracy of High Resolution Computed Tomography in Diagnosing Cholesteatoma, taking Histopathology as Gold Standard.*

We have conducted this study to determine the diagnostic accuracy of high resolution computed tomography in diagnosing cholesteatoma, taking histopathology as gold standard. Age range in this study was from 12-50 years with mean age of 27.72 ± 10.24 years. Majority of the patients 31.54% were between 12-20 years of age. Out of these 130 patients, 73(56.15%) were males and 57(43.85%) were females with ratio of 1.3:1. All the patients were subjected to high resolution computed tomography scanning of temporal bone and HRCT scan supported the diagnosis of cholesteatoma in 73 (56.15%) patients and no cholesteatoma in 57 (43.85%) patients. Histopathology findings confirmed cholesteatoma in 74 (56.92%) patients and no cholesteatoma in 56 (43.08%) patients. In HRCT positive patients, 69 (True Positive) had cholesteatoma and 04 (False Positive) had no cholesteatoma on histopathology. Among 57, HRCT negative patients, 05 (False Negative) had cholesteatoma on histopathology whereas 52 (True Negative) had no cholesteatoma on histopathology (p=0.0001). Overall sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of high resolution computed tomography in diagnosing cholesteatoma, taking histopathology as gold standard was 93.24%, 92.86%, 94.52%, 91.23% and 93.08% respectively.

One study has shown the sensitivity and specificity of high resolution computed tomography in diagnosing cholesteatoma as 89.29% and 77.22% respectively.[9] In a study of 64 patients with middle ear cholesteatomas, Gaurano and Joharjy found that the diagnosis of these cholesteatomas was suggested by specific characteristics found on CT scans. These included expansion of the aditus and mastoid antrum (92% of patients) and ossicle erosion (also 92% of patients). Preoperative CT scans in the study had 97% correlation with surgical and histopathologic findings.[10]

Mafee et al repoted in their series of 48 patients with cholesteatoma that 46 of them (96%) had been diagnosed correctly with preoperative HRCT.[12] Chee et al concluded in their series of 36 patients that 34 patients (94.4%) had been correctly diagnosed by HRCT.[13] Joselito et al reported in their series of 64 patients that the analysis of the preoperative HRCT scan correlated with the surgical findings and histopathologic reports with a high degree of accuracy (96.8%).[14] Hassman et al in a series of 60 patients reported that there is good correlation between HRCT findings and operative features in cholesteatoma for most middle ear structures.[15]

HRCT had sensitivity of 100%, specificity of 100%, positive predictive value of 100%, and negative predictive value of 100% in predicting the cholesteatoma. This finding is in agreement with that of Walshe et al[16] and Sirigiri and Dwaraknath[17] who reported a sensitivity of 90% and 87.5%, respectively. Chee et al concluded in their series of 36 patients that 34 patients (94.4%) had been correctly diagnosed by CT.[18] Joselito et al reported in their series of 64 patients that the analysis of the preoperative CT scan correlated with the surgical findings and histopathologic reports with a high degree of accuracy (96.8%).[14]

A study showed a high incidence of cholesteatoma in the third decade of life. The scutum and lateral attic wall were the most common bony erosions in the middle ear bony wall (64.3%), and the incus was the most eroded ossicle in the middle ear (88.2%). Sclerosing of mastoid air cells were encountered in 60.7% of patients and the lateral semicircular canal was affected in 9%, while facial canal erosion was found in 21.4%. Temporal bone complications are more common than intracranial complications. HRCT findings were compared with operative features; the comparative study included the accuracy and sensitivity of HRCT in detecting cholesteatoma (92.8%), its location and extension (96.4%), ossicular chain erosion (98%), labyrinthine fistula and intracranial complications (100%).[19]

CONCLUSION

This study concluded diagnostic accuracy of high resolution computed tomography (HRCT) in diagnosing cholesteatoma is quite high. So, we recommend that this non-invasive and easily available technique should be done for pre-operative assess-

ment of cholesteatoma and selection of proper surgical approach in order to reduce the morbidity of these particular patients.

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Limitation of Study Surgeries were performed by ENT surgeons with variable clinical experience.

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Conflict of Interest The idea presented in this article is solely of the authors and is in no direct conflict to any individual or institution.

Ethical Issue According to the authors there is no ethical issue in this study.

Authors Contributions

Conception & Design Dr. Naeem Ahmad Khan.

Collection & Assembly of data Dr. Naeem Ahmad Khan, Dr. Tanweer Ahmad.

Literature Review & Critical Revision of the article for important intellectual content Dr. Tanweer Ahmad, Dr. Basma Khan, Dr. Adnan Ahmad Sattar, Dr. Fatima Iqbal, Dr. Shehzad Masood.

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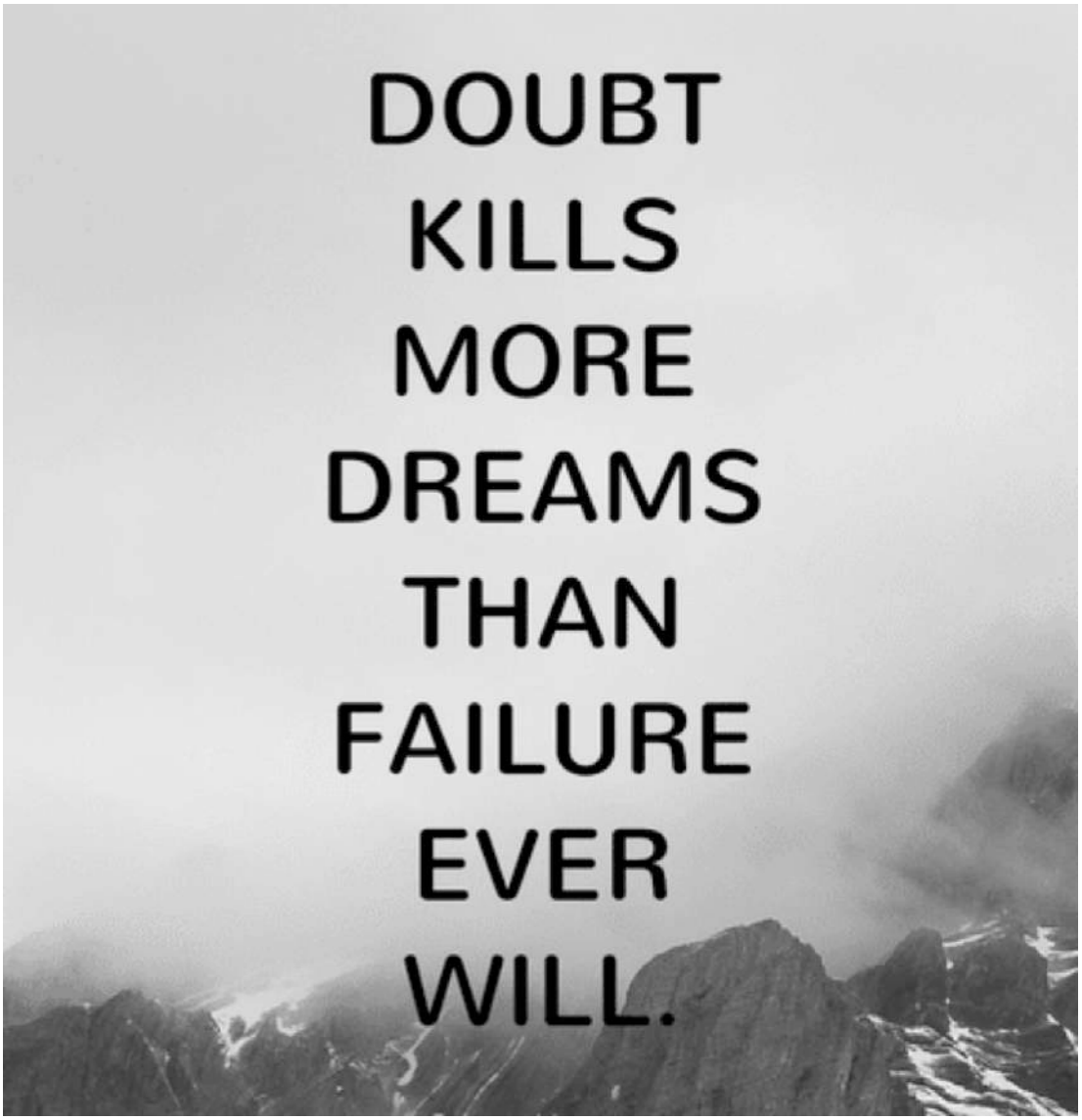

FREQUENCY OF DEPRESSION IN MEDICAL STUDENTS

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Abstract

Background: Depression can hamper the social, professional and physiological functioning. Medical students are considered more under stress than general population. However, various frequencies of depression have been reported at different setups. So, we conducted the study reassessed the frequency of depression among medical students in our setup.

Objective: The objective is to determine the frequency of depression among the medical students. It was an observational cross sectional survey, conducted at the Department of Psychiatry and Behavioral Sciences, Allama Iqbal Medical College/Jinnah Hospital, Lahore

Methodology: This study included 400 medical students. The main outcome variable was frequency of depression among these medical students which was detected by using Agha Khan University Anxiety and Depression Scale (AKUADS). A score of 19 was taken as cut off point. The depression was described through frequency distribution table.

Results: Out of 400 medical students, 152 (38%) medical students were detected to have depression while the rest of 248 (62%) medical students did not have depression.

Conclusions: The frequency of depression among medical students is high. So, it should be evaluated among all medical students.

Key Words: Depression; medical students

The goal of medical education is to train knowledgeable, competent, and professional physicians equipped to care for the nation's sick, advance the science of medicine, and promote public health. Medical schools undertake an extensive selection process to identify intelligent and altruistic individuals with a strong commitment to these goals and then spend five years trying to prepare those individuals to achieve them.[1]

In many countries, the systems of medical education typically begin after candidates have achieved a degree that includes at least basic training in biology, chemistry, and physics, as well as training in the humanities. Applicants typically must undergo standardized examinations and a rigorous application and interview process. In addition to identifying individuals with the necessary aptitude and commitment to pursue a career in medicine, this process is intended to identify individuals who choose to pursue a career in medicine based on significant insight into the demands, challenges, and rewards of the profession. Once enrolled, students and schools make a mutual commitment intended to prepare students for a socially useful and personally fulfilling career.[2] Depression is a disabling disorder that can disrupt an individual's occupational, social, and physiological functioning. The lifetime prevalence of major depression is estimated at 16% in the general population.[3] In many cases (20 –30%)

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symptoms of depression persist for years, often without remission.[4]

Depression is common problem (prevalence in general population ranges from 6 -17%)[5] which may present as an independent as well as co-morbid condition.[6]

Medical students represent a group thought to be at particular risk for developing depression and emotional disorders.[7] Indeed, depression is one of the most common psychiatric disorders affecting university students, with current prevalence rates estimated at 10% in undergraduate samples. This is most likely related to academic, financial and social demands that college environments place on students at a time when they are also involved in issues related to life style and careers.[8,9] Possible causes of student distress include adjustment to the medical school environment, ethical conflicts, exposure to death and human suffering, perception of being taken advantage of or abused, and recent stressful life events.[10,11]

Additional stresses of medical school include heavy workloads, academic pressures, a competitive environment, limitations on personal time, and financial burden.[12] In addition to depression and anxiety, potential consequences of student distress include impaired academic performance, cynicism, academic dishonesty, substance abuse, and suicide. Mental health problems in medical students may correlate with medical doctor's relatively high suicide and drug addiction rates.[13,14]

Different frequencies of depression among medical students have been reported in different studies. In a study by Amir, M et al.[15] it is 28 % and in study by Mehanna, Z et al. it was 27%. In a local study by Jadoon N. A, et al. the frequency of depression among medical students was 43.89% which was diagnosed on Aga Khan University Anxiety and Depression Scale (AKUADS).

A longitudinal study shows that burnout (49.6%), quality of life an depressive symptoms predict suicidal ideation (11.2 %) in the following year. This even leads to suicidal attempts in 2.7% of medical students.[9] This issue needs to be addressed and students should be encouraged to seek help along with provision of adequate facilities.

The rationale of this study indicates variability among data about frequency of depression in medical students which has been observed in different studies, so the researcher reassesses it. This would highlight the magnitude of the problem and would guide us in making policies for screening of depression among medical students and to put services in place to help them.

The objective of the study was to determine the prevalence of depression in medical students.

METHODOLOGY

It was an observational cross sectional survey, at the Department of Psychiatry and Behavioral Scien-ces, Allama Iqbal Medical College/Jinnah Hosptial, Lahore. The calculated sample size was approximately 400 cases with 5 % margin of error, 95 % confidence level taking expected percentage of depression among medical students i.e. 43.89%. Duration was six months from June 2006 to November 2006, with non-probability purposive sampling.

Inclusion Criteria

- Gender: both male and female
- Age: 18 – 28 years
- Medical students were included in study after six months of getting admission in MBBS.

Exclusion Criteria

- Medical students with diagnosed medical illnesses e.g. hypothyroidism, epilepsy (were excluded on the basis of history and clinical examination)
- Medical students with previous history of psychiatric illness like bipolar affective disorder, schizophrenia (were excluded on the basis of psychiatric history and Mental Status examination).
- Medical students who had history of substance abuse e.g. cannabis, alcohol (based on history).
- Chronic fatigue syndrome assessed on history
- Past history of depressive illness

Four hundred cases fulfilling inclusion criteria were enrolled from Allama Iqbal Medical College, Lahore after an informed consent. The inclusion of student's data in this study was obtained after ensuring them total confidentiality. Psychiatric semi-structured interview conducted in privacy. Their demographic data like age, gender, address was obtained and recorded on Performa (attached) by self administrated. To avoid observed bias and confounders were controlled by strictly following exclusion criteria. All the medical students were assessed by AKUADS for depression. The medical students were labeled with depression as per operational definition and the score on AKUADS was mentioned on Performa. All the data was collected on Performa.

All the collected data were entered into SPSS version 10 and analyzed. The qualitative data like demographics (sex; male or female) and depression (Yes or No) were presented as frequency distribution. Quantitative data in the study like age (in years) were presented as means and standard deviations.

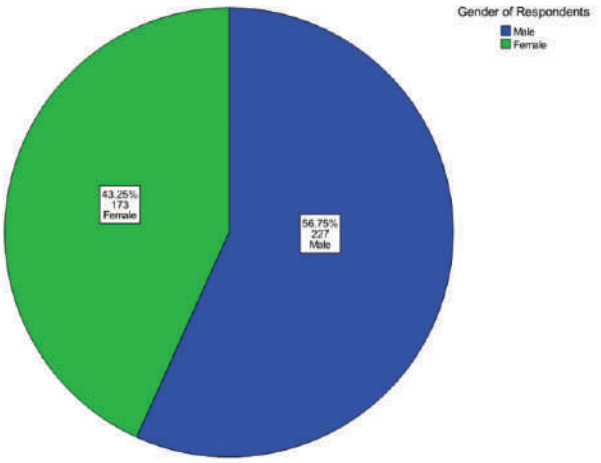
RESULTS

400 medical students were recruited for the study. The mean was 21 years, maximum age was 24, minimum age 18 years and standard deviation was 71.785.(Table 01). 43.2% were males and 56.8% were females (Graph no:01). Scoring on AKUADS was done, the mean score is 24.2, median score 23.0, mode 13.0, minimum score is zero, maximum score 81% and standard deviation is 15.7%.(Table no:02).

Frequency and percentage among subjects on AKUADS was 44.5% normal. 42.5% were mild, 9.3% have moderate, 3.0% have severe, 0.8% have very severe depression.(Table no:03). Age wise distribution on AKUADS Scale, age between 18-24 years, normal score (age 18-20 years was 41.7%, age 20 to 22 years was 47.4%, 22-24 years 45.0%). Mild score was(in age 18-20 was 42.3%, age 20-22 was 45.9% in age 22-24 was 38.5%), moderate score (age 18-20 was 12.2%, age 20 - 22 was 4.4% in age 22-24 was 11.0%), severe score (in age 18-20 was 3.8%, age 20-22 was 2.2% age 22-24 was 2.8%) very severe score (in age 18-20 is .0% in age 20 -22 was.0% in age 22 -24 was 2.8) (Table no: o4).

Table 1: *Age of Respondents*

Statistics		
Age of Respondents		
N	Valid	400
	Missing	0
Mean		21.12
Median		21.00
Mode		23
Std. Deviation		1.785
Minimum		18
Maximum		24



Graph 1: *Gender of Respondents*

On AKUADS cross tabulation was done between gender distribution, normal score in males was 38.3%, in females 52.6%, mild score was in males 44.1%, in females 40.5%, moderate score in mlaes 13.7% in females 3.5%, severe score in males 4.0% in females 1.7%, very severe in males 0.0% in females 1.7%

Table 2: *Scoring of AKUADS*

Statistics		
Scoring of AKUADS		
N	Valid	400
	Missing	0
Mean		24.27
Median		23.00
Mode		13
Std. Deviation		15.711
Minimum		0
Maximum		81

(Table no: 05). Mean scoring of AKUDAS was compared among male and female medical students. Mean AKUDAS among males was 23.0 and among females was 19.0.

DISCUSSION

This study was conducted in a Psychiatry Unit of teaching hospital to detect the frequency of depression among medical students. The results of this study showed a higher prevalence (38%) of depression among medical students.

In literature, there are many studies that have described the frequency of depression among medical students. However, the results of these studies are variable with each other. This may largely be due to the methodology and criteria used to diagnose depression.

In a local study by Jadoon NA, et al.[17] which was conducted at Nishtar Hospital, Multan, which is a teaching institute, 815 medical students were evaluated for the symptoms of depression. Out of 815 students, 482 completed the questionnaire with a response rate of 59.14%. The mean age of students was 20.66 ± 1.8 years. A high prevalence of anxiety and depression (43.89%) was found amongst medical students. Like our study, they used Aga Khan University Anxiety and Depression Scale with a cut-off score of 19. The results were comparable to our study with a higher frequency of depression. Frequency and percentage among subjects on AKUADS was 44.5% normal. 42.5% were mild, 9.3% have moderate, 3.0% have severe, 0.8% have very severe depression. (Table no: 03).

Khan MS, et al. 83 also conducted a study at a private institute of Pakistan. The mean (SD) age of the students was 21.3 (1.88) years. Majority of the students were females. A very high prevalence of anxiety and depression (70%) was found among students. Like our study, they used the similar criteria for the diagnosis of depression i.e. Aga Khan University Anxiety and Depression Scale with a cut-off score of 19. They observed a very high frequency of depression among medical students. This may be attributed to the increased economic burden of a private medical college as the students have to pay more in terms of college fees and dues.

Inam SNB, et al. 84 conducted another cross sectional study which was done on the students of Ziauddin Medical University, which is also a private medical college. The instrument used to assess the anxiety and depression levels was the, Aga Khan University Anxiety and Depression Scale (AKUADS). Of these 189 were present during the survey, it was found out that 113 (60%) students had depression which is again a higher frequency than ours. This also validates the results of study by Khan MS, et al, which showed a higher frequency of depression among students of a private medical college as compared to the government hospitals.

Zaid ZA, et al.[7] also conducted a study in a private medical school among 292 medical students. The students completed the 12-item English version of the General Health Questionnaire (GHQ-12) and a demographical questionnaire. A cut-off point of 3/4 for the GHQ was used to establish the diagnosis of depression. Out of 292 medical students, 86.6 percent completed the questionnaires. A total of 117 students (46.2 percent) were found to have depression.

Dahlin M, et al. 85 conducted a study which was carried out at the Karolinska Institute Medical University, Stockholm, Sweden. Matched controls from the general population were used. There were 342 medical students included in this study. The response rate was 90.4%. They found that the prevalence of depressive symptoms among students was 12.9%, which was quite lower than ours. The results of their study showed a decreased frequency of depression than ours, but they also concluded that frequency of depression was quite higher among their medical students than the general population.

In my study age wise distribution was also done that showed distribution on AKUADS Scale, age between 18-24 years, normal score (age 18-20 years was 41.7%, age 20 to 22 years was 47.4%, 22-24 years 45.0%). Mild score was (in age 18-20 was 42.3%, age 20-22 was 45.9% in age 22-24 was 38.5%), moderate score (age 18-20 was 12.2%, age 20 - 22 was 4.4% in age 22-24 was 11.0%), severe score (in age 18-20 was 3.8%, age 20-22 was 2.2% age 22-24 was 2.8%) very severe score (in age 18-20 is .0% in age 20 -22 was.0% in age 22 -24 was 2.8) (Table no: o4).

This study has certain limitations. Although we did the randomization of the medical students, this represents a population of a single center. This also highlights the need for more clinical traits at multiple centers to cover the actual population.

CONCLUSION

The frequency of depression among medical students is high in our study so it is recommended to evaluate this problem among the medical students.

We also suggest for multicentre, clinical trials to validate the observed frequency in our study. Moreover hospital guidelines and policies should be established to recognize the problem. Limitations of study:

Our study being a cross sectional study has a limited value regarding evidence based medicine. We would also like to replicate the study in other cities to see if there are any differences in prevalence rates or associated factors of depression.

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Conflicts of Interest None

Funding sources None

Authors Contributions

All six authors have contributed equally in conceptualization and detailed work of our project.

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ASSOCIATION OF DYSLIPIDEMIA WITH SEVERITY OF PSORIASIS

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Abstract

Objectives: To evaluate the association of dyslipidemia with severity of Psoriasis.

Methodology: A cross-sectional survey was carried out on psoriasis patients presenting in dermatology department. A total of 120 adult patients with psoriasis of either sex were included in this study. All of the study population was advised for a mandatory 12 hours fast before taking samples for Total Cholesterol, Triglycerides, Low density lipoproteins and High density lipoproteins.

Results: The mean duration of disease in our study population was 5.46 ± 4.49 years. Majority of the patients had moderate diseases based on PASI with mean PASI score being 14.98 ± 8.95. Mean age of the patients was 38.59 ± 13.86 years with an overall male predominance as 78 (65%) out of 120 patients were males and 42 (35%) being females. Of these, 67 (55.8%) patients had dyslipidemia whereas 53 (44.2%) patients had normal lipid levels. Total cholesterol (T.C:>200mg/dl) was elevated in 34 (28.3%) patients. 32 (26.7%) patients had raised low density lipoprotein cholesterol (>130 mg/dl) while 44 (36.7%) patients had Hypertriglyceridemia (TG: >150 mg/dl). Meanwhile, reduced high density lipoprotein-cholesterol levels (HDL C:<40mg/dl) was observed in 35 (29.2%) patients.

Conclusion: it is concluded that severity of psoriasis was associated with higher risk of dyslipidemia. Significant number of patients with psoriasis had dyslipidemia. Therefore, all patients with psoriasis should be evaluated and if needed, treated for dyslipidemia.

Key Words: Dyslipidaemia, Hyperlipidemia, Psoriasis.

Psoriasis is a chronic, disfiguring, inflammatory and proliferative condition of the skin. The characteristic lesions of psoriasis consist of red, scaly, sharply demarcated, indurated plaques, most commonly involving scalp, elbows, knees, hands, feet, trunk, and nails. It affects 1-3% of world's population.[1] As per World Psoriasis Day Consortium, about 125 million people across the globe have this disease.[2] Age at onset of type-1 psoriasis is between 15-30 years and it is HLA associated while type II psoriasis appears after 40years and lacks HLA association.[3] The etiology of psoriasis includes genetic, autoimmune and environmental factors. The locus, psoriasis susceptibility 1(PSORS1) located in the major histocompatibility complex (MHC) genes is the major genetic determinant for psoriasis. Autoimmune mechanism is mediated through T-cell activation and secretion of type-1(Th-1) cytokines e.g. interferon γ, interleukin-2 and tumor necrosis factor alpha (TNF-α).[4] These cytokines induce inflammatory changes in epidermis producing thick scaly red plaques and in some patients, arthritis.[5]

Environmental factors like streptococcal pharyngitis, stressful life events, drugs, HIV infection, trauma, smoking and alcohol consumption[6,7] have been associated with psoriasis and psoriatic arthritis.[8]

Psoriasis is associated with an abnormal plasma lipid metabolism and it has been observed that lipid levels are raised in patients with psoriasis.[4,9,10] Total

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cholestrol, triglyceride and low density lipoprotein (LDL-C) haveall been found to be elevated in psoriatic patients. However High density lipoprotein (HDL-C) is either unaffected or reduced.

Since dyslipidemia is one of the criteria for diagnosing metabolic syndrome, psoriasis is also found to be associated with metabolic syndrome.[11,12] Insulin resistance can lead to type 2 diabetes mellitus in psoriatic patients.[13] In one study dyslipidemia was found in 50.9% of the patients with psoriasis.[11] Other co-morbid factors increasing the risk of dyslipidemia include higher body mass index (BMI) >30, family history of dyslipidemia, sedentary life style, high fat diet, and patients taking retinoid or cyclosporine for the disease. The chronic inflammatory nature of psoriasis along with dyslipidemia have been suggested to be contributing risk factors for the development of co-morbidities like atherosclerosis, coronary artery disease and myocardial infarction resulting in increased cardiovascular mortality.[14,15,16]

There are multiple reasons for dyslipidemia associated with psoriasis. The molecular and physiologic changes in digestive system, immune mechanism involving IL-6,TNF-alfa & CRP[17] along with cellular oxidative stress may be responsible for altered lipid metabolism. Auto antibodies against oxidized LDL have been detected in psoriatic patients.[9] Dyslipidemia not only promotes atherosclerosis but also maintain the inflammatory reaction in the skin.[18] The level of antibodies against oxidized LDL have been found to correlate with disease severity. Because of this dyslipidemia and inflammatory state, patients with psoriasis are at high risk of developing metabolic syndrome, atherosclerosis, coronary artery diseases, and associated myocardial infarction as compared to general population. Dyslipidaemia in psoriatic patients is often overlooked and untreated. Since dyslipidaemia is the independent risk factor for cardiovascular events, dermatologists should consider it in order to enhance early assessment of cardiovascular risk and mortality.

The association of dyslipidaemia with psoriasis has been established in various international studies.[9,10,11] But to date only limited number of local studies are available to establish an association between psoriasis and dyslipidaemia.[4] This study was aimed at determining the frequency of dyslipidemia in psoriatic patients in our setup. In general, patients with psoriasis are not screened for dyslipidemia because often their primary disease is considered relatively less life threatening. However, as dyslipidemia is amongst the preventable as well as treatable risk factor of deadly ischemic heart disease, the main objective of this study was to determine the frequency of dyslipidemia in psoriatic patients in our setting.

It is, therefore, hoped that by regular screening, we may be able to benefit the patients by diagnosing and treating dyslipidemia early and in turn this will contribute towards improving the quality of life and minimizing the cardiovascular mortality and morbidity.

Psoriasis: Diagnosis based on clinical finding of well demarcated symmetrical red papules & plaques with silvery scales involving the extensor surfaces and scalp.

Dyslipidemia: Diagnosed biochemically from serum taken after 12 hours fasting. Subjects were considered to have dyslipidemia if any of the following four criteria was present. Total Cholesterol ≥200 mg/dl, Triglycerides ≥150mg/dl, Low Density Lipoproteins-Cholesterol ≥130mg/dl(LDL-C),High Density Lipoproteins-Cholesterol(HDL-C) <40mg/dl (males) <50mg/dl (females)

METHODOLOGY

This cross- sectional study was conducted at a dermatology department of a tertiary care hospital. Using non probability sampling a calculated sample size of 120 cases was taken, with 9% margin of error and 95% confidence interval taking expected percentage of dyslipidemia to be around.

Patients of psoriasis, both male and female, between 15-70 years of age (as defined in operational definition) with all grades of severity i.e. mild, moderate and severe were enrolled. Obese patients (high BMI >30kg/m^2) and those having diabetes mellitus, chronic renal failure, chronic liver disease

and hypothyroidism diagnosed on urine analysis, fasting and random blood sugar levels, renal function tests, liver function tests and thyroid profile, history of alcohol consumption, family history of dyslipidemia, patients taking drugs like beta blockers, thiazides, corticosteroids, cyclosporine, retinoids and lipid lowering drugs for six months (on history/previous medical record)and pregnant females or those taking oral contraceptive pills for six months were excluded.

One hundred and twenty 120 patients, who met the inclusion and exclusion criteria were enrolled after the informed consent. A detailed demographic detail such as name, age and gender was taken from patients. After an overnight fast (12hours), the patients were asked to return early in the morning and their intravenous blood sample about 3cc was sent to Pathology Laboratory for estimation of total cholesterol (TC), triglycerides (TG), low density lipoproteins (LDL-C) and high density lipoproteins (HDL-C). The report was assessed for the presence or absence of dyslipidemia. All the information was entered in a structured Performa.

Data was entered and analyzed in SPSS version 13.0. Numerical variable like age was presented as mean and standard deviation. Gender and presence or absence of dyslipidemia was presen-ted as frequency and percentage. Age (15-30 years, 31-45 years, 46-60 years and above 60 years), gender (male, female) and psoriasis area and severity index i.e. PASI score (Mild <7, moderate 7-12 and severe >12) acted as effect modifiers and were addressed through stratification.

RESULTS

The mean age of the patients in the study was 38.59 ± 13.86 (range 15-70 yrs). Out of the total 120 patients, 78 (65%) were male patients and 42 (35%) were female patients. The mean duration of psoriasis was 5.46 ± 4.49 years.

Figure 01 shows out of the total 120 patients, 67 (55.8%) patients had dyslipidemia and 53 (44.2%) patients had normal lipid levels.

Table.01 shows the association of dyslipidemia with severity of Psoriasis. Disease severity was assessed by psoriasis area and severity index i.e. PASI score. The mean PASI score was 14.98 ± 8.95. Out of 120 patients 30 (25%) patients had mild psoriasis i.e. PASI <7, 30(25%) patients had moderate psoriasis i.e. PASI 7-12 and 60(50%) patients had severe psoriasis i.e. PASI >12. Incidence of dyslipidemia was directly proportional to the severity of disease.

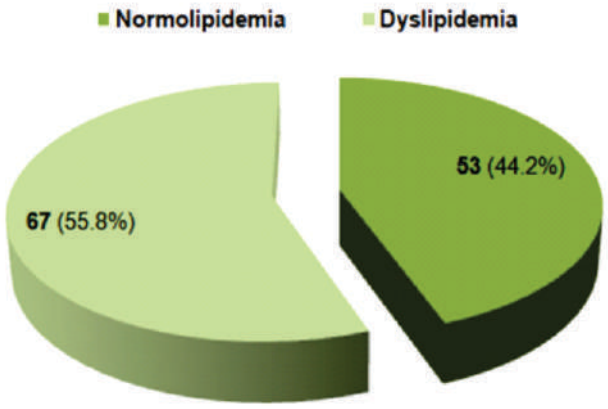

Figure.1: *Frequency of Dyslipidemia*

DISCUSSION

Psoriasis is a chronic, disfiguring, inflammatory and proliferative condition of the skin. Psoriasis has been associated with an abnormal plasma lipid metabolism and serum lipid levels are raised in patients with psoriasis.[4,9,10] Total cholestrol, triglyceride and low density lipoprotein (LDL-C) has been found to be elevated in psoriatic patients. High density lipoprotein (HDL-C) is either unaffected or reduced. Since dyslipidemia is one of the criteria for diagnosing metabolic syndrome, psoriasis is also found to be associated with metabolic syndrome.[11,12] Insulin resistance can lead to type-IIdiabetes mellitus in psoriatic patients. The chronic inflammatory nature of psoriasis and dyslipidemia have been suggested to be contribu-

Table 1: *Association of Dyslipidemia with Severity of Psoriasis*

	Disease Severity		
	Mild (PASI<7) **(n=30)**	**Moderate** (PASI 7-12) **(n=30)**	**Severe** (PASI>12) **(n=60)**
Dyslipidemia	07(23.3%)	10(33.3%)	50 (83.3%)
Normolipidemia	23 (76.7%)	20 (66.7%)	10 (16.7%)

ting risk factors for the development of co-morbidities like atherosclerosis, coronary artery disease and myocardial infarction resulting in increased cardiovascular mortality. [14,15,16]

When we compared our results with other studies, it was found that in our study the mean age of the patients was 38.59 ± 13.86. In the study of Bajaj DR et al,[4] the mean age of patients was 37 ± 7.96 years and in the study of Akhyani M et al,[9] the mean age was 41.18 ± 17.37 years. These are quite comparable with age range of our study population.

In the present study, there were 65% male patients and 35% female patients, while in the study of Javidi Z et al[19] there were 56.7% males and 43.3% females. The mean duration of psoriasis was 5.46 ± 4.49 years as compared with the study of Bajaj DR et al[4] the mean duration was 4.5 ± 1.89 years.

The association between psoriasis and dyslipidemia has also been somewhat controversial in past. We found a strong association as 55.8% of the psoriatic patients had altered lipid levels, consistent with the studies of Cohen AD et al[11] where it was present in 50.9% patients and of Dreiher J et al[10] where dyslipidemia was found in 57.1% of psoriatic patients. However, in contrast, studies done by Neimann AL et al[20] and Farshchian M et al[21] have failed to find a consistent association.

Among many case control studies on serum lipid levels in psoriasis, conflicting results have been reported regarding serum cholesterol, LDL-C, serum triglyceride and HDL-C levels. Total cholesterol and LDL-C levels in psoriatic patients were found to be either significantly higher[4,9,19,22] or similar[10,21,23] to controls. Triglyceride levels were reported to be significantly higher[4,9,10,19] in psoriatic patients in some studies, but not in other studies.[21,22,23] Finally, HDL-C levels had been found to be significantly lower,[10,24] similar [4,9,19,21,22] or even higher[23] to controls. As our study was a cross-sectional study, therefore, P values could not be calculated. We found hypercholesterolemia in 28.3%, raised LDL-C in 26.7%, hypertriglyceridemia in 36.7% and low HDL-C in 29.2% of psoriatic patients.

Although female patients presented to us were less in number (35%) as compared to male patients (65%) but the females were found to be more dyslipidemic (64.28%) than males (51.28%). This finding is contrary to the study of Bajaj DR et al[4] who found dyslipidemia in males more than the females.

Dyslipidemia was found more frequently in the patients with severe psoriasis. It was observed that in the patients with mild psoriasis i.e. PASI<7, 7(23.3%) had dyslipidemia as compared to the patients with severe psoriasis i.e. PASI>12, 50(83.3%) had dyslipidemia. Thus, frequency of dyslipidemia increased proportionately with the severity of disease. Javidi Z et al[19] found that total cholesterol levels significantly increased with disease severity. LDL-C levels also increased but not significantly, while serum triglyceride and HDL had no relation with disease severity. Contrary to this, Mallbris L et al[23] did not observe any significant association between disease severity and lipid profile.

According to a survey done at Agha Khan hospital 31% of normal ambulatory Pakistanis had dyslipidaemia[25] while our study showed 55.8% psoriatic patients had dyslipidemia. This shows that psoriatic patients have a much higher incidence of dyslipidemia as compared to normal Pakistani population.

Psoriatic patients with dyslipidemia are at high risk of developing the metabolic syndrome, atherosclerosis and myocardial infarction. Therefore, serum lipid levels should be routinely measured in every psoriatic patient in our setup so as to reduce the cardiovascular mortality and morbidity.

CONCLUSION

It is concluded from this study that significantly higher proportion of patients with psoriasis have dyslipidemia (55.8% in our study). Not only this, but also, severity of psoriasis was associated with higher risk of dyslipidemia. Therefore, it is important that serum lipid levels should be routinely measured in all the psoriatic patients so as to identify dyslipidemia early and to possibly avoid& if needed treat possibly fatal cardiovascular complications.

Conflicts of Interest Authors declare no conflict of interest.

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Contribution of Authors Jamil, A. is the corresponding author. Rest of the authors contributed equally.

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COMPARISON OF TWO REGIMES OF HELICOBACTER PYLORI ERADICATION IN PREGNANCY WITH HYPEREMESIS GRAVIDUM IN PAKISTANI POPULATION

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Abstract

Objective: The aim of this study is to look for the clinical response of the two regimes of Helicobacter pylori (H. Pylori) eradication in pregnant ladies having hyperemesis gravidum (HG).

Methodology: 130 pregnant ladies having HG after informed written consent were given either conventional treatment or the standard pharmacological treatment and after 2 weeks clinical response was evaluated.

Results: The group receiving the standard treatment of H. Pylori eradication for HG showed significant benefit in clinical response as compared to the counterpart.

Conclusion: The significant improvement in the HG symptoms in pregnancy with standard treatment not only showed the beneficial effect of the treatment but also a clear association between the occurrence of HG and the H. pylori infection.

Key Words: Helicobacter, Hyperemesis, Pregnancy, Vomiting

Hyperemesis Gravidum (HG) is a common problem affecting around 0.3-2% of pregnancies.[1] When nausea vomiting is associated with loss of weight, electrolyte disturbances, ketonemia, elevated liver enzymes, it is defined as Hyperemesis gravidum.[2] This effects the general wellbeing as well as the quality of the life of the pregnant ladies[3] and in severe cases need hospitalization and may lead to death.[4]

Being more common in 1st trimester, cause of HG is not that much obvious and clear.[5]

It may be multifactorial ranging from endocrine disorders, gastrointestinal disorders and psychological issues during the pregnancy to even unknown condition yet to be discovered.[6,7]

Helicobacter pylori (H. pylori) is a very common infection in Pakistan which ranges from asymptomatic to various clinical presentations like peptic ulcer, chronic gastritis and even cancer.[8]

H. pylori is a spiral shaped, flagellated gram negative bacteria[9] leading to cytokine related inflammation and gastrin release in gastric mucosa along with decreased secretion of bicarbonate leading to acidification of duodenum and the resulting clinical manifestations.[10] H. pylori is a potential causing factor of HG and it has been shown by various studies as well.[11,12,13]

The severity of the symptoms vary among individuals and is mainly related to the amount of the bacterial amount infected as also shown by a study.[14]

There are few therapies available for the eradication of H. pylori each having different potencies, side effects and complications.[15]

Pregnancy being a very delicate matter needs cautious use of medicines requiring effective as well as safe treatment on the same hand. Currently the

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following study is conducted to assess the clinical benefit of the two regimes: one is proper diet, intravenous fluids, vitamins supplements, electrolyte replacement and anti-emetics while the other regime included all of the above plus proper high dose of Amoxicillin and Lansoprazole for two weeks. Currently no such study has been conducted in our population.

METHODOLOGY

The study is done in Hayat memorial Hospital / Continental Medical College, Lahore from September 2019 till Dec 2019 recruiting 130 pregnant ladies having age 26±2.1 years. All patients were having HG with persistent nausea and vomiting and having weight loss > 2kg and ketonemia. The weight measurements were done initially at the first visit in 1st trimester followed by the subsequent antenatal visits.

Inclusion Criteria

1st trimester

Positive Fecal antigen test (FAT) for H. pylori antigen in stool by enzyme immunoassay and having symptoms of HG

Exclusion Criteria

Liver or Gastrointestinal disorders

Psychological issues

Treatment with antibotics within last 7 days

H/o of Peptic Ulcer

Contraindications to use of PPI or Amoxycillin

Gestational trophoblastic disease

It is a randomized control study approved by the ethical board review of the Jinnah Hospital/ Allama Iqbal medical college, Lahore.

Demographic information like name, age was obtained. A detailed history both general, drug (recent intake of antibiotics or PPI within 7 days) as well as gynecological along with abdominal examination was done. An ultrasound was done to look for viability of fetus, rule out multiple gestations and gestational trophoblastic disease.

Complete Laboratory investigations (CBS, LFTs, T3, T4, TSH, RFTs and Serum electrolytes) were done to rule out exclusion criteria likes Liver, Gastrointestinal disorders, Thyroid dysfunction and any coexisting infection. Ketones in urine as diagnostic criteria for HG was also done.

All patients were admitted in the antenatal ward of the hospital. The patients were divided randomly in two groups. Group A having 64 patients received the conventional treatment (Diet instructions, intravenous fluids, electrolyte replacement, anti-emetics and vitamins supplementation) while Group B having 66 patients received High dose treatment in the form of Lansoprazole 30mg TID 30minutes before meals + Amoxicillin 1gm TID 30minutes after meals for 2 weeks. Both Lansoprazole and Amoxicillin are category B drugs. The patient's response to treatment was evaluated after two weeks in the form of stoppage of vomiting, improvement in oral intake and weight and general wellbeing. All the data was entered and analyzed in SPSS version 22. Data were expressed as frequency and percentage for qualitative variables and mean + standard deviation (SD) for quantitative one. P value of < 0.05 considered significant.

RESULTS

All the enrolled patients completed the study. Regarding the demographic and clinical characteristics there was non-statistical difference between the two groups as shown by the table 1. The patients tolerated the treatment regimens well with minimal side effects and no patient left the treatment. In Group A, only 32% of the patients got clinical improvement while the remaining 68% patients remained symptomatic. On the other hand the clinical improvement was remarkable in the Group B with 86% of the patients showing clinical benefit having P value of 0.002 and only 14% didn't have any improvement.

The cases in Group A which didn't improve were then offered the high dose treatment given to Group B. Those cases who didn't improve by either treatment were then kept under observation with strict monitoring and treatment.

DISCUSSION

The prevalence of H. pylori infection is higher in developing countries as compared to the develo-

Table 1: Demographic and Clinical Characteristics of Group A & Group B

Variable	Group A 64 Mean ± SD	Group B 66 Mean ± SD	P value
Age	26.3±2.5	26.6±2.9	0.1
Duration of vomiting	7.4± 1.6	8.3±1.2	0.23
Gestational Age	13.4±1.3	11.7±1.2	0.23

Table 2: Response of Treatment between Two Groups

Variable	Group A 64	Group B 66	P value
Clinical improvement	21 (32%)	57 (86%)	0.002
No Clinical Improvement	43 (68%)	09 (14%)	

ped countries[16] which may be due to poor hygiene, low socioeconomic status etc.

HG being a very common and disturbing problem in early pregnancy needs proper management. There is clear association of H. Pylori infection in causing HG shown by various studies.[17,18]

There are many factors which lead to increase susceptibility of H. pylori infection in pregnancy like shift in body fluid PH, hormonal changes leading to increase in the symptoms of nausea and vomiting.[19]

Previously many studies have been done showing good results of the treatment regimens but these were done in non-pregnant ladies.[20]

Our study, to our knowledge, is the first study done in our population in pregnant females evaluating the response of the high dose regimen. There are different treatment regimens used which have various drug combinations. A study done using ranitidine, metronidazole and ampicillin for 14 days showed an efficacy rate of 66.6% in symptom improvements both clinically as well objectively.[21]

Another study used a combination of omeprazole, metronidazole and amoxicillin with good relieve of symptoms but in contrast to our study this was done in the last trimester of pregnancy unlike the 1st trimester where the teratogenic fear is the most. [22]

This study used omeprazole as one drug which is not licensed to be used in pregnancy though didn't reveal any increase in congenital or pregnancy related complications. [23]

A study done by Labenz et al. done in 1999 used two drugs, a PPI and amoxicillin to eradicate H. pylori in pregnant ladies with relative good success but with a condition if the PH of the gastric mucosa is > 5.5.[24]

In our study, two drugs were used with high dose of amoxicillin with a relative more effective PPI Lansoprazole[25] showing greater efficacy, better clinical outcome. In Group A, only 32% patients got improvement with the traditional treatment leading to hypothesis that simple symptomatic measures are not sufficient for the management of this condition. The other supporting point was drawn from the fact that the Group B had 86% of the patients getting improvement with the use of antibiotic regimen along with symptomatic management so the role of H pylori as an infecting agent is definite.

The fact that this regimen lead to almost no side effects make it also very safe and reliable management plan, while other regimens using quinolones and tetracycline are contraindicated in pregnancy because of teratogenicity and their safety is not well established[26] So it can be said safely that H. pylori is a definite risk factor for HG and definitely requires treatment. High dose Amoxycillin and Lansoprazole appears to be very effective and safe in eradication as well clinical improvement of the symptoms of HG.

Limitation of the Study

Small sample size remains a limitation of the study rendering low power of the finding. Further study on larger population is required.

Conflict of Interest

All authors declare no conflict of interest.

Funding Source

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Contribution of Authors

Dr. Iram Inam: Concept: Data Collection, Proof reading

Dr. Nadim Yousaf: Sample Collection

Dr. Ghias-ul-Hasan: Sample collection, Data interpretation

Dr. Aqsa Khalid: Paper writing, Similarity index

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IMPACT OF COVID-19 ON CLINICAL PRACTICE OF ORTHOPEDIC SURGERY

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Abstract

Background: In medical science when new techniques, High end innovations and robotic surgery were ruling the roost from conventional methods with all specialties growing in to super specialties. The biological danger induced by Covid-19 brought the world to stand still.

So the fear and danger exerted by this virus has turned the world upside down. Regarding Covid-19 the human life was limited up to the protective measures.Covid-19 has affected the medical practice without any doubt. Similar is the situation in orthopedic field, so the whole orthopedic field and clinical practice has been pushed into state of hibernation with dormant redundancy.

Objectives: This study was conducted to assess the impact of Covid-19 on clinical practice in different orthopedic institutes of the country.

Methodology: An online survey was conducted by emails send to orthopedic surgeon in different part of Pakistan. A total number of 240 orthopedic surgeons participated in the survey. The duration of the study was from August 10th, 2020 to August 25th, 2020. A questionnaire to assess the pre-Covid-19 and post-Covid-19 clinical orthopedic practice.

Results: This prospective study shows that the orthopedic surgeon's management plan was adopted to respond more effectively to Covid-19 pandemic while maintaining the standard of health care and protection of medical staff and patients. Out of 240 participants 196 orthopedic surgeons participated in the survey with response rate of 82%. 52% were the senior surgeons while 48% were the junior orthopedic surgeons. Among these of total 82%, 72% declared that clinical practice was dropped by 70% during this pandemic. While drop in practice at DHQs and THQs was 68% and in private clinics the drop in practice was 50%. None of the surgeons became Covid-19 positive. 80% of the surgeons continue to attend orthopedic trauma during the pandemic by adopting PPE's.

Conclusion: It was concluded from our study that covid-19 has drastic effects on the clinical orthopedic practice. To continue outpatient consultation and operative procedures, although long term after effects cannot be elucidated at the moment, the implementation and availability of PPES and awareness regarding the covid-19 infection should be ensured. Limitation of hospital resources and availability of ICU bed for covid-19 should be a priority and proper planning should be employed judiciously to continue the orthopedic clinical practice.

Key Words: Covid-19, orthopedic surgeons, pandemic, global spread, orthopedic trauma

In Dec 2019 an outbreak of coronavirus disease 2019 (COVID-19) was first detected in Wuhan in china SARS-COV-2 is highly infectious and is suspected to spread from bat to humans.[1] This new virus SARS-Cov-2 was the cause of these calamity and has been called as corona virus disease 2019 (COVID-19) SARS-COV-2 is a single strand RNA virus structurally similar to other corona viruses, has three viral proteins, membrane (M), spike(S), and envelope (P). On Jan 30th, 2020 this was declared as public health emergency of international concern by international health regulation committee of WHO. Furthermore on March 11, 2020 it was declared as global pandemic.

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Because of this global pandemic, Pakistan suffered from this highly infectious disease as its border is connected with Iran and China. First confirm case of this disease was reported in Pakistan on Feb 26, 2020 in Karachi. The virus spread nationwide and has currently become pandemic. Confirm total cases are 416,499 and 8361 deaths resulted from corona virus.[2]

The mode of spread is from person to person as a social contact, social gathering and overcrowding by droplets infection. The clinical features depends upon the severity and age long standing chronic illness and associated comorbidities.[3] There is progressive respiratory distress resulting in respiratory failure that can end up in mechanical ventilator support. When the disease is severe, it can result death of the patient.[4]

In 80% of the patients COVID-19 is asymptomatic or it causes minor illness.

As there is no specific treatment exist for this new calamity, the only hope is protective measures either restriction of movements or effective lockdown enforced to control the spread of infection, Personal protective equipment (PPE's) like face mask, face shields, gloves, gowns and other protective measures especially for health professionals. Even these measures although very effective still they are not 100% successful to prevent the spread of COVID-19 infection.[15]

There is still incomplete understanding of the disease caused by this virus. Moreover the disease can presents in different ways with or without respiratory problems.

Like all other surgeries, the elective orthopedic surgical procedures were postponed and number of indoor and OPD patients were considerably decreased to limit the spread of infection associated with COVID-19.[5,6] Although orthopedic surgeons are not the front line workers as compared to infectious disease consultants, medical specialist, pulmonologist and acute critical care consultants. However as a part of large health care system, orthopedic consultants have a vital role regarding the protective measures against this COVID-19 pandemic.[14]

Because of high level of awareness among the orthopedic surgeons risk of COVID-19 can be minimized by the health care providers to the patients by adopting the international guide line against COVID-19. In this way the pre-operative and post-operative chances of infection can be reduced or minimized.[11] Since this is a new disease and still the complete understanding of the disease processes is deficient.[13] COVID-19 has high infectivity and fatality rate than H1N1` epidemic. Most of the orthopedic surgeons are unwilling to operative the COvid-19 positive patients because of risk to get the infection themselves its spread to their families and the community. This has results marked decreased in orthopedic clinical practice by emergent of this decreased outbreaks.[12]

These protective measures have decreased the risk of contaminated COVID-19 positive patients and allow the hospitals to free bed for medical management of COVID-19 patients.

Moreover the number of hospital visit was decreased and non-urgent visits were reduced to avoid the overcrowding and flow of patients and therefore minimizing the risk of infection. All these patients were provided facility of telemedicine.[9,10]

Data also reveals the willing of orthopedic surgeons and support their professional challenges in ICU if it is required.

METHODOLOGY

This descriptive study was carried out to analyze the impact of covid-19 on orthopedic clinical practice of orthopedic surgeons practicing in Punjab. Data was collected by online survey from 240 orthopedic surgeons practicing at 30 different tertiary care hospitals, DHQs, THQs and Private hospitals. The duration of study was from august 10, 2020 to august 30, 2020. A questionnaire was prepared to assess the impact of covid 19 on the clinical practices in last 6 months. The drafted questionnaire was circulated among orthopedic surgeons via email, WhatsApp and mail. Out of 240 only 196 orthopedic surgeons sent the feedback.

One hundred and ninty six orthopedic surgeons responded and partici-pated in the study. All the data was collected via questionnaire distributed via email, whatsapp and mail. The data was analyzed by SPSS version 17.

RESULTS

Out of 240 orthopedic surgeons 196 participated in this study. The response rate was 82%. The average age of the surgeons was 48 years (35 to 75 years). Major share was from the junior orthopedic surgeons (60%) working in tertiary care teaching institutes. 10% share was from the orthopedic surgeon working in the DHQs and 7% from THQs while it was 5% from private clinics.

Out of 60%, the job description of 50% was Assistant Professors, 7% was Associate professor while 3% were the professors. Of the remaining 22%, the senior consultants at DHQs and THQs were 17% and Private clinics consultants were 5%. Majority of the surgeries done were related to trauma of the limbs.

Out of 196 participants, 72% (141 surgeons) reported that their outdoor practice has dropped to 70% (p-value<0.001). Practice drop in teaching institutes was 70% and also dropped to 68% in DHQs and THQs. The surgeons working in private clinics reported that their clinical practice has reduced to 56% (p-value <0.001)

Out of 82% (196 surgeons), 10% of our surgeons did not attend the trauma patients after the onset of COVID-19 pandemic. There was also reduction of volume of surgery. The surgeon who operated 20 cases per month was operating 15 cases per month. All elective surgeries like arthroplasty, spine and reconstructive procedures were either cancelled or postponed due to non-availability Or limited availability of PPEs.

After the onset of pandemic the number of trauma patients presenting in the emergency were reduced to 40% (p-value<0.0001). Among trauma patients presented in emergency mostly were young's (60%), while the 30 % were of middle age and the remaining 10 % were of old age.

Table 1: *Number of Elective Operative Procedures Performed during COVID-19 and Pre-COVID-19 Period at Tertiary Care, DHQs and THQs*

Elective Surgeries	No. of Surgeries during the Pre - COVID period (Last 06 months)	No. of Surgeries during the COVID-19 period (06 months)
Arthroplasty	72	18
Spine	13	02
Soft-tissue procedures	60	30

Table 2: *Number of Emergency Operative Procedures Performed During COVID-19 and Pre-COVID-19 period at Tertiary care, DHQs and THQs*

Emergency Procedures (Trauma)	No. of Surgeries during the Pre - COVID period (Last 06 months)	No. of Surgeries during the COVID-19 period (06 months)
Upper limb	788	504
Lower limb	792	552

DISCUSSION

Covid-19 has drastically affected surgical field including orthopedics clinical practice. An online survey was performed to assess the impact of covid-19 on orthopedic specialty.[1] The bio-danger induced by covid-19 brought the fear and scared the whole world including Pakistan. Because of increase mortality rate and associated severity of infection induced by COVID – 19, it has affected the whole healthcare system including Orthopedic & Trauma surgery.[2,3,4,5]

In our study 72% of surgeons reported that their OPD patients have been reduced to 70%.The study done by Haffer et al, also favor the reduction in clinical in orthopedic practice.[16]

The response rate by orthopedic surgeons in our study was 82% which was a good sample to study the real impact of covid-19. This also shows the interest of this specialty doctors towards this calamity. The experience of 75% of orthopedic surgeons was more than 15 years. It is obvious that most of these surgeons had excellent pre covid-19 clinical practice. So collecting the data from such experienced persons can really reveal the clear picture of the existing problem.[17]

In most of the hospital staff was divide into two group's one half of the doctors serving the orthopedic patients in the department and the other half was speared to serve the COVID-19 patients. Similar option was adopted at services hospital. The shortage of Para-medical staff was also there due to lack of transport facility during effective lockdown. Road traffic accidents were also reduced because of limited mobility of the people on roads. The reason for increase in rate of hip fractures in old population was that most of the old population stayed at the home and it was home emergency injuries that required the orthopaedic intervention. 2nd in number were the open fractures which were not of same magnitude as per pre covid-19 but still they fall in the 2nd position.[6,8]

No surgeon contracted the covid-19 infection. This was because of safe preventive measures like social distancing and PPES which were followed by surgeons in most of the consultation area. The surgical procedures done by most of our consultants were also limited and most of the surgeons performed less than 3 procedures in a single week. No one operated more than 07 procedures per week. It was because of reduction in manpower and optimal conditions during the COVID period. As available staff had no clear cut and definitive knowledge of operations theatre SOPs and lack of PPE. Moreover during the orthopedic procedures, use of electric cautery, orthopedic drills and cutting saws were the causes of spread of the infection. The surgeons who operated during this period were the real frontline workers during the pandemic with limited resources.[3,4]

The elective orthopedic surgeries were either postponed or were limited and 45.91% of our surgeons operated less than 2 cases per week (Arthroplasty, Spine surgery, soft tissue reconstructive procedures and complicated trauma). Remaining 54 % of (106 Surgeons) of the surgeons who attended the trauma treated most of their patients with POP cast and back slabs with limited visits of the patients to the hospital except those patients who underwent surgical procedures. These patients were given online advice regarding their further management except those patients who needed in-hospital visits[18,19]. In our clinical practice at SIMS/ Services Hospital, most of the OPD patients were provided with the facility of telemedicine.[9,10]

15% of our respondents got covid-19 infection, although in almost all the hospital it was mandatory to get covid-19 test prior to surgery.[13,14,15] This shows that even adherence to safety guidelines and implementation of protective measures, a person can get infection and that may be due to exposure with asymptomatic patients or operating the asymptomatic covid patients with less proper PPE.[11,12,20] Study of Guo et al. at Wuhan shows that risk of orthopedic surgeons of getting infected with covid-19 was 1.5-20.7%, who did not performed the covid-19 test for their patients.[21]

Ethical Approval by the hospital committee was not required as this study was not conducted on the patients.

Limitation of study

Very few articles have been reported in Pakistan regarding the impact of covid-19 on orthopedics clinical practice. No of orthopedic surgeon were limited in our study. A larger group of surgeons should be included in the study. Moreover we did not interpret the management protocols and practical guidelines and disease pattern to prevent the impact of Covid-19 at orthopedic clinical practice.

CONCLUSION

It was concluded from our study that covid-19 has drastic effects on the clinical orthopedic practice. To continue outpatient consultation and operative procedures, although long term after effects cannot be elucidated at the moment, the implementation and availability of PPES and awareness regarding the covid-19 infection should be ensured. Limitation of hospital resources and availability of ICU bed for covid-19 should be a priority and proper planning should be employed judiciously to continue the orthopedic clinical practice.

The protection of surgeons and healthcare worker should be preferred at all levels. Planning the surgery and care of patients with covid-19 disease should

have a clear roadmap

Although orthopedic surgeons do not directly treat the covid-19 disease but their exposure to corona patients cannot be ruled out while treating the patients presenting after trauma. They are under direct exposure in emergencies are facing increased pressure due to this Pandemic.

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Conflict of Interest Author declared that there is no conflict of interest.

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FLIPPED CLASSROOM: ATTITUDES OF STUDENTS TOWARDS AN INNOVATIVE PEDAGOGY IN A PUBLIC SECTOR MEDICAL COLLEGE

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Abstract

Objectives: To assess the attitudes of students towards introduction of Flipped Classroom methodology to be incorporated in credit hours of medical education. A cross-sectional study based on results derived from questionnaires given out to students of Allama Iqbal Medical College, Lahore

Methodology: Sample size was calculated by OpenEpi Software Online, keeping the frequency of anticipapted factor (awareness of flipped classroom) to be 38% and confidence level 95%. The value of "n" came out be 300. Completely filled forms by undergraduate medical students were included. Data entry and analysis was conducted using SPSS 21.

Results: During the current divisive academic climate, it was surprising to note that majority of the learners feel the need to adopt a new teaching approach. This should be taken into consideration and applied to update our medical education system. The only minor resistance to this change were digital disparity that the online teaching system creates, level of teacher training that differs on various levels and the degree of awareness related to the enquiry.

Conclusion: This study concludes that the majority of students have positive attitudes towards adopting an innovative teaching methodology; Flipped Classroom.

Key Words: Flipped Classroom, Inverted Classroom, Online Teaching, Video Lectures, Digital-Divide, Medical Students, Homework, Learning pace, Long-Term Memory

In a conventional instructor – focused classroom, the teacher delivers lectures during class time and gives students homework to be done after the class. In a flipped, or inverted, classroom, things are done the other way round: the teacher "delivers" the lectures before class in the form of pre-recorded videos, and spends class time engaging students in learning activities that involve collaboration and interaction.[1]

The term "inverted classroom" appeared in the literature as early as 2000 by Lage, Platt and Treglia.[2] It was made popular by Chemistry teachers Bergmann and Sams in recent years.[3]

One of the most frequently mentioned success stories are the Khan Academy and Massive Open Online Courses – the flipped classroom gained attention at educational institutions in North America across a myriad of disciplines and at various stages of instruction. This pedagogy has also been regularly regarded as one of the top trends in educational technology.[4]

Some tutors have testified lower failure rates[5], superior flexibility, reduced stress[6], improved student sensitivities and even better test scores,[7] for classrooms that embraced this model.

However, being a relatively new trend, most implementations of the flipped classroom are reported

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in blogs, online magazines and newspapers instead of academic papers and conferences. There seems to be little rigorous research done to measure the effects of this teaching methodology, and what has been published so far seems far from conclusive. [8]

There is data available on the effectiveness of the pedagogy. A 3-year-long study of flipped learning for a pharmaceutics course reported a 5.1% improvement in student performance by Meyer in 2013.[9] Contradictory preliminary data from another 3-year study at Harvey Mudd College suggest that flipping may not cause any difference in student outcomes.[10] Adding to the debate, a recent study by Schnieder et al., concludes that students who engage in open-ended exploration first outperformed those who used traditional textbook materials first, and implies that video lectures and textbooks should come after exploration, and not before. [11]

The effectiveness of this method can be tested out as an interventional study performed on on-going classes in undergraduate medical colleges in Pakistan, but before that the readiness of students to adopt this as a tutorial method needed to be surveyed. This study was intended to explore the views of medical students regarding a completely new or perhaps 'unheard-of' tutorial induction and subsequently make an informed medical education related decision.

METHODOLOGY

A cross-sectional study design was adopted to determine the perceptions of students towards the possibility of introduction of Flipped Classroom in medical colleges. The duration of study was one month – from 15th January to 15th February 2020 – that was conducted in Allama Iqbal Medical College, Lahore.

Sample size was calculated using the OpenEpi online source at 95% Confidence Level and by using an anticipated frequency 38% {Awareness regarding Flipped Classroom} and that came out to be, n=300. 12 Completely filled forms, by MBBS students enrolled in aforementioned institute, were included in the study. Forms that were partially filled or filled by Allied Health Sciences students were excluded.

A brief description pertaining to the innovative method was written, for the responder, preceding the questionnaire in order to familiarize and then expect a reasonable opinion. Students were allowed ample time to fill up the forms. In order to modify the questionnaire in an indigenous context, 30 forms were distributed randomly among equal number of male and female students. Feedback of responders was collected in the form of suggestions and subsequently classified and updated in the final questionnaire. This pre-testing allowed to reform the questions to be used for the final survey.

After modification, a questionnaire containing 32 closed-ended questions was presented to the responder that they filled-out themselves, and analyzed their views about flipped classroom.

Data entry and analysis was performed using the SPSS 21 software. Frequency and percentage of variables were tabulated and the results were analyzed.

RESULTS

Eleven key questions were extracted from the inquiry form and frequency tabulations for 300 complete responses were included, i.e. awareness of flipped classroom approach at the day of filling the survey form, learning at students' own pace, possibility of developing long term memory, digital divide, whether conducive for students with mental challenges, allowance of gadget use by parents, preparation for flipped classroom can be home work itself, congruency of professional examination with the new method, variability of facilitators regarding training to hold a successful flipped classroom, whether the students themselves are willing to be prepared for a flipped classroom and, finally, the likelihood of trial of this technique in Pakistan.

Awareness Factors

Seventy two percent(216) out of the total students were unaware of the concept about Flipped Classroom.

The opinion of students regarding the coherence of university annual examinations with the tutorial

method being surveyed, depicted a varied response

Table 1: Flipped Classroom: Attitudes of Medical Students Towards the Introduction of Flipped Classroom in a Public Sector Medical College

Sr. No.	Question	Variable	Frequency	Percent
1.	Before today did you have any knowledge of "Flipped Classroom" methodology of teaching or have ever participated in one?	Yes	84	28.0
		No	**216**	**72.0**
2.	Do you think "Flipped Classroom" can create a Digital Divide?	Strongly Disagree	14	4.7
		Disagree	19	6.3
		Neutral	62	20.7
		Agree	**127**	**42.3**
		Strongly Agree	78	26.0
3.	Do you think Flipped Classroom methodology is considerate of students with mental challenges?	Strongly Disagree	21	7.0
		Disagree	63	21.0
		Neutral	**94**	**31.3**
		Agree	89	29.7
		Strongly Agree	33	11.0
4.	Do you think Flipped Classroom can be difficult for you because you are not allowed to use the computer or gadgets by your parents, for too long?	Strongly Disagree	37	12.3
		Disagree	**90**	**30.0**
		Neutral	60	20.0
		Agree	80	26.7
		Strongly Agree	33	11.0
5.	Do you think your current professional annual examinations are designed in such a way that would require and introduction of Flipped Classroom as a medium of instruction?	Strongly Disagree	36	12.0
		Disagree	50	16.7
		Neutral	86	28.7
		Agree	**97**	**32.3**
		Strongly Agree	31	10.3
6.	Do you think that participating in every Flipped Class you have with your teachers/facilitators will be at the same level of intensity and productivity?	Strongly Disagree	39	13.0
		Disagree	**93**	**31.0**
		Neutral	76	25.3
		Agree	72	24.0
		Strongly Agree	20	6.7
7.	Do you think Flipped Classroom concept should at least be tried before completely labelled as not applicable for Pakistan?	Strongly Disagree	13	4.3
		Disagree	16	5.3
		Neutral	60	20.0
		Agree	**151**	**50.3**
		Strongly Agree	60	20.0

spread over "agreed" and "neutral", 32.3% and 28.7%, respectively (Table 1).

Technology Factors

Any online medium of instruction can create a digital-divide amongst students from various socio-economic backgrounds and hence it is reflected in the frequency for this factor (Table 1). 42.3% (127) and 26% (78) agreed and strongly agreed over this issue.

Whether parents will allow this much time to indulge in working on computers or other gadgets is also debatable. The results showed a widely distributed frequency pattern over all the options given to the responders. 30% (90) disagree with this being an issue, whilst 26.7% (80) agree (Table 1).

Hindrance Factors

Results for mental challenges creating a double-burden on students, if the practice of flipping the classroom begins, displayed the highest percentage in the "neutral" option (31.3%). Although 29.7% (89) students agreed as well and 21 (7%) strongly agreed (Table 1).

Perceptions of students pertaining to the ability of their instructors to hold a triumphant flipped class is significant based on the results that 44% (132) agreed or strongly agreed with the notion. 30% disagree and reflect their faith in their teachers (Table 1).

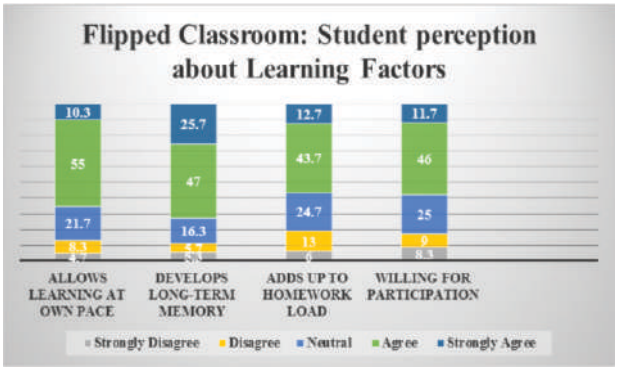

Fig. 1: *Learning-Based Perceptions of Undergraduate Students Regarding Flipped Classroom Introduction in a Public Sector Medical College*

Whether or not this method should be tried before completely discarding it for implementation in Pakistan also does not have very surprising results. 50.3% (151) agree and 20% (60) strongly agree that it should be put to trial, at least (Table 1).

Learning Factors

Regarding the autonomy of learning pace and increasing long-term memory, through flipped classroom technique, exhibited profoundly conspicuous frequencies amongst students. 165 students (55%) agreed that the new method will allow learning at students' own speed. 141 students (47%) agreed and 77 (25.7%) strongly agreed with the ability of the new teaching way in increasing long-term memory (Fig. 1).

Majority of the responders agreed (47%) and/or strongly agreed (12.7%) with the fact that inverted classroom method increases burden in the form of home work. Even though the technique involves eliminating the concept of traditional homework style but, nevertheless, preparing for a flipped class is homework as well (Fig. 1).

Upon asking whether the students are themselves motivated enough to carry out the preparation that goes into participating in a flipped class, 138 (46%) agreed and 35 (11.7%) strongly agreed and 17.3% (Fig. 1) disagreed or strongly disagreed.

DISCUSSION

The awareness regarding flipped classroom method is ubiquitously undermentioned in statistical data for even teachers in Pakistan, let alone students who are studying in their formative years of medical education.[13] Do all students, recruited for medical colleges in Pakistan, come from economically the same backgrounds or is there a heterogeneous distribution of social classes among potential doctors? The answer is predominantly from lower socio-economic strata.[14] Therefore an expectation of awareness about a first-world pedagogy is unrealistic. Our results reflecting a significantly higher frequency of students who do not have any information about flipped classroom is comparable with results from Jaster RW. In 2017.[15]

Moreover, according to students (128, 42.6%) the quality of questions they attempt in the annual professional examinations is complex enough and requires an update in teaching methodology. One of the reasons why this could be a conflicting result is because the data was also collected from first year medical students who still have not appeared for a final examination at the university level or maybe a multifactorial recline from educational activities in generation alpha.[16] A local study published in 2020, tested the difficulty index, discrimination index, cognition level and distraction efficiency employed at the University of Health Sciences, Lahore, and has recommended improvement in all the fields.[17] Yet most of our students have agreed to embrace flipped classroom to better prepare themselves for the professional examinations, even though acceptable results could be achieved by traditional methods.

A paper published in 2018 discussed three different discourses pertinent to global poverty and responsibilities of higher education in relation to it. One of the disruptive potentials of online teaching, especially in developing countries, is that it creates a disparity amongst students from various socio-economic backgrounds.[18] 68.3% of our respondents agree with the aforementioned possibility as a genuine concern. Our results are consistent with another study by Block J. that mentions that purchasing expensive gadgets is probably not the only reason why technology-assisted teaching techniques can be problematic but also training of end-users is required to commence at a primary education level, in a developing country.[19]

Out of 300 students that we surveyed, 38.7% agreed and 32.3% disagreed with the enquiry about whether their parents would be comfortable with their child spending too much time on computers. Perceptions of parents or guardians, related to online teaching ways, are still very orthodox and will evolve over time. Nevertheless, our results are similar to various international publications about this issue. In a report by Kanthawongs P. in 2013 it was reported that parents only allow two hours per day for their child to indulge in technology, whether or not it is for academic purposes.[20] The reason for our responses spread over all categories of agreement is probably the fact that majority of our students are boarders.

Three of the recorded factors are classified as

hindrance contributors to any kind of basic change in medical education. Namely, mental health challenges to cope with a new learning strategy, whether the institute will provide with technologically sound and trained faculty and whether a country's population is ready for a change or not. As far as psychological challenges are concerned, the highest percentage recorded was for 'neutral' (30%), which was expected – as mentioned in a study by Papish A. et al in 2013 – because of stigma associated with reporting mental issues amongst post-pubertal age bracket individuals.[21] Reportedly the burden of medical education, all through undergraduate training, is already substantial and therefore our results are inconsistent with this fact.[22]

In a comparative study analyzing current problems with the prerequisites for flipped classroom, done in China, groups of students were allotted to different teachers to check for their individual approach towards the new teaching method. Two turned out to exhibit markedly progressive results while three had a relatively lower percentage of leading-in questions, in-depth analysis and participation in difficult exercises, from the students' point of view. It is quite mundane to realize that not all teachers are capable of establishing quality standard required for a flipped class.[23] Forty four percent (132) of the responders disagreed when asked if their teachers are equally qualified to run a flipped class, according to our results.

Should flipped class pedagogy be at least tried, first, before being labelled as not applicable for Pakistan and its' response from students is quite pertinent, since they are the key clientele. An overwhelming majority of 70% (211), based on our results, reflected agreement – congruent with several studies from across the globe.[24,25,26,27]

Our results for whether this technique allows learning at students' own pace (Agreed; 65.3%) are akin to a paper by Nouri J.[28] Whether it is conducive for developing long-term memory (Fig. 1), as agreed by 72.7% of our respondents is comparable to countless publishes, internationally. For instance in a study published by Hew and Lo in 2018.[29]

Preparation for flipped classroom, once and if adopted, will increase the burden of homework, substantially, is an obvious preconceived idea. This reflected in our results with 56.4% (169) of responders agreeing to it (Fig. 1) and matches with several international publications that based on interventional studies.[30]

Finally, preparing for flipped class requires a lot of effort on both the students' and teachers' end. Since we were establishing students' opinions for this survey, a need to enquire about whether our pupils be onboard was relevant. 57.7% agreed to embrace it, provided that the motivation is ample. Research originating from various academic institutes, across the world, have reported similar results.[31,32,33]

CONCLUSION

In conclusion, the concept of Flipped Classroom or Inverted Classroom is a relatively new one for a country like Pakistan that already has many hurdles to overcome as far as education is concerned. Perceptions and assumptions of medical educators, regarding their target audience and their responsive attitudes towards learning, are vague and inappropriately generalized. Our study shows that our students are relatively more open-minded, towards accepting learning challenges, that we give them credit for. Students generally want to give flipped classroom a try, are motivated enough to actively participate, do believe that the method enhances long-term memory and allows learning at one's own pace, and, the need for teachers to catch up with new technology trends. An interventional study must be conducted to assess the degree of improvement in learning among medical students.

Limitations of Study

- Gender based opinions not collected.
- Sample population from one public sector medical college.

Acknowledgments

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Conflicts of Interest None

Funding Source None

Contribution of Authors

Dr. M. Qasim Muneer: Writing abstract, introduction, materials and methods, results, discussion, conclusion and referencing.

Dr. Kanwal Saeed: Interpretation of results and introduction writing.

Dr. Munazza Sardar: Interpretation of results and reporting results.

Prof. Mah Jabeen Muneera: Discussion and conclusion writing.

Hadia Younis: Data collection and entry.

Saad Saqib: Data collection and entry.

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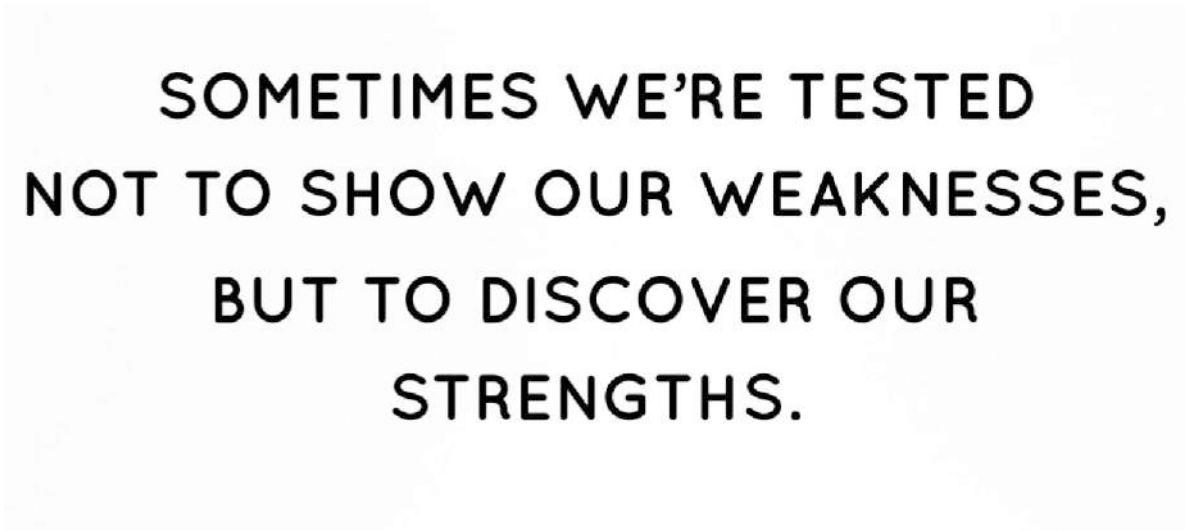

CLINICAL AND LABORATORY FEATURES OF MULTIPLE MYELOMA PRESENTING AT A TERTIARY CARE HOSPITAL

Farah Arif,[1] Ayesha Khalid,[2] Rabia Ahmad[3]

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Abstract

Background: Plasma cell Myeloma, constitutes about 15% of the hematological malignancies and the annual incidence of 1% of all malignancies1. It is currently incurable and occurring with increasing frequency in older population. Clinical features which are present in majority of the patients are bone pain, pallor due to anaemia, weakness, renal failure or insufficiency, fatigability and symptoms of hypercalcemia. Incidental discovery on comprehensive laboratory panels is common. Diagnosis of multiple myeloma is confirmed by serum or urine protein electrophoresis or immunofixation ,serum free light chain ratio and bone marrow aspirate examination2 .Few myelomas are light chain myelomas, which constitute about 10% cases of plasma cell myeloma. In these cases only monoclonal Ig light (L) chains are produced. Such chains are found minimally in plasma as they can pass glomerular filters, precipitate within renal tubules and be recovered in urine as dimers (Bence Jones (BJ) protein (BJP)2. Plasmacytoma (< 5% of plasma cell disorders) can be either a single bone or extramedullary plasmacytoma . For diagnosis of plasmacytoma ,biopsy confirmation of a monoclonal plasma cell infiltrate is required3.

Objective: The objective of this study was to evaluate the laboratory and clinical features of newly diagnosed patients with plasma cell myeloma (PCM).

Methodology: This study was carried out at Allama Iqbal Medical College Lahore, from October 2005 to January 2010.

Thirty two newly diagnosed cases of multiple myeloma were included in this study. Relevant findings in history, physical examination and laboratory findings were analyzed.

Results: In this study among 32 patients, 17 were males and 15 were females with mean age 52.8 ± 9.3 years. The common complaints were bone pain and backache. The common clinical findings were pallor and high ESR (ESR of all the study patients was more than 100 mm in 1st hour). Mean Hemoglobin level was 8.1 g/dL±1.5 . Hypercalcemia was noted in 6 patients. Mean calcium was 9.3±1.5 mg/dl .Lytic lesions were the most common radiological finding in the study.

Conclusion: Multiple myeloma or plasma cell myeloma is a disease of the middle and elderly aged population with relative preponderance of males. Bone pain is the predominant symptom in majority of patients. Hypercalcemia may not be present in most of the patients.

Key Words: Multiple myeloma, plasma cells, lytic lesions

Plasma cell myeloma is a hematological neoplasm characterized by proliferation of monoclonal plasma cells derived from B cells. Monoclonal plasma cells proliferate in the bone marrow and affect the adjacent bone by release of some mediators, producing destruction of bony skeleton resulting in bone pain and fractures. Monoclonal plasma cells produce M protein and monoclonal light chains and it may lead to renal failure from monoclonal light chains or Bence Jones protein or hyperviscosity due to increased monoclonal proteins in the blood. The diagnosis requires meeting the criteria of International Myeloma Working Group[1]. Plasma cell myeloma is approximately 1% of neoplastic diseases and 15% of all hematological malignancies. The median age at diagnosis is approxi-

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mately 60-70 years. In a study, about 37% of patients are less than 65 years, 26% are between the ages of 65 and 74 years, and 37% are older than 75 years.[3]

Although the exact causative factors of plasma cell myeloma are not known, exposure to some viral infections, ionizing radiation, farming pesticides, petrochemicals increase the risk. Inidence also increases in autoimmune disorders like Rheumatoid arthritis[3]. People with Rheumatoid arthritis or obesity have an increased incidence of multiple myeloma (a BMI of over 30 kg per square meter). Secretion of cytokines and growth factors, , like interleukin-6, tumor necrosis factor, TGF β1, and interleukin-10, VEGF and insulin-like growth factor 1, is increased in multiple myeloma. Myeloma is either asymptomatic or symptomatic, due to the absence or presence of organ or tissue dysfunction, hypercalcemia, renal dysfunction, anemia, and lytic bone lesion or fracture[3]. Approximately 34% of patients are asymptomatic at presentation with incidental abnormalities on total protein, creatinine, calcium or hemoglobin laboratory panels. Anemia, which is present in about 73% of patients at diagnosis, is generally related to myeloma marrow infiltration or renal dysfunction. Bony lesions develop in almost 80% of patients with newly diagnosed disease; in one study, 58% of patients reported bone pain[3]. Renal impairment occurs in 20 to 40% of patients with newly diagnosed disease, mainly as a result of direct tubular damage from excess protein load, dehydration, hypercalcemia, and the use of nephrotoxic medications. The risk of infection is increased with active disease but decreases with response to therapy. Hypercalcemia is uncommon. Serum β2-microglobulin and albumin are two most important prognostic factors. The International Staging System defines three risk groups on the basis of these two. Myeloma is usually incurable. In recent years, the introduction of autologous stem cell transplantation and the availability of agents such as thalidomide, lenalidomide, and bortezomib have changed the management of myeloma and extended overall survival[2]. In patients presenting at an age under 60 years, 10-year survival is approximately 30%[3]. Therefore, the purpose of this study was to determine the spectrum of clinical, hematological and biochemical changes in the patients of multiple myeloma..

METHODOLOGY

This study was carried out from Oct 2005-Jan 2010 in Allama Iqbal Medical College/Jinnah Hospital Lahore. In this study the total number of cases was 32. Diagnosis was based on serum protein electrophoresis, bone marrow examination and FNAC from plasmacytoma. Relevant clinical history, physical findings, complete blood count and ESR, bio-chemical tests like serum albumin, serum calcium, serum creatinine, serum β2 microglobulin and radiological survey were recorded for further analyses.

RESULTS

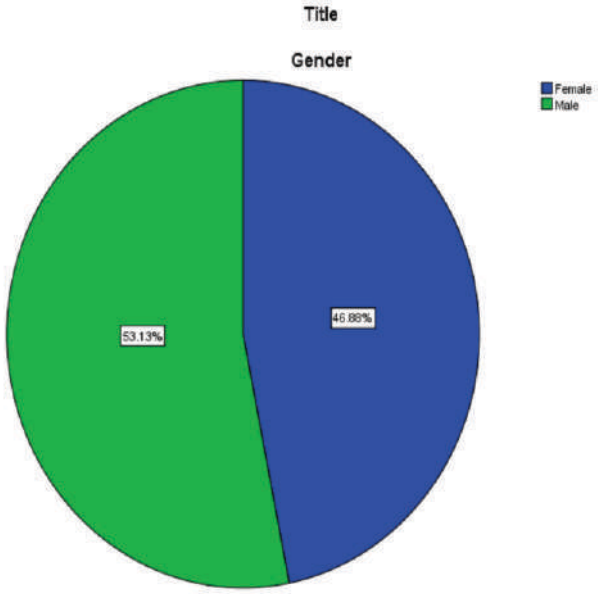
Total 32 patients diagnosed as multiple myeloma were included in this study. Out of them 17 (53%) were males and 15 (47%) were females with male female ratio 1.2:1. Age range of patients was 30−68 years with mean 52.81 ± 9.36 years and median 53 years. Bone pain, weakness and fatigue were the most commonly presented complaints. Bone tenderness and anemia were the common clinical findings. No organomegaly or lymphadenopathy was found. Investigations revealed that mean Hb level was 8.1± 1.5 g/dL . Mean WBC count was 5.7l±2.7×10^9/l and mean Platelet count was 192±108×10^9/l .The mean calcium level was 2.1±1.8 mg/dL. Mean S. albumin level was 2.6±0.7g/l. Diagnostic criteria of multiple myeloma were fulfilled by all 32 patients in this study. Frequency of different symptoms and signs were noted. Majority of the patients had bone pain i.e;20 out of 32 patients presented with bone pain, while headache was present in 2 patients only. 26 patients were pale, splenomegaly was noted in 1 patient, while hepatomegaly was noted in 2 patients.

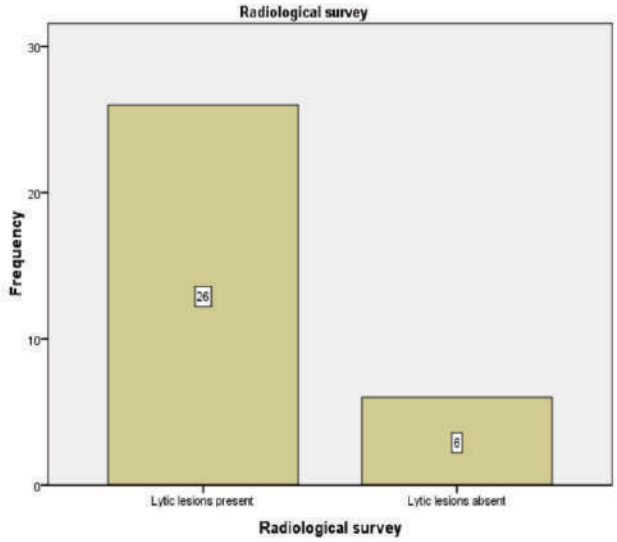
There was no significant difference between either gender and either bone pain or lytic lesions, p values=0.5 and 0.07 respectively. There was also no significant difference between both genders and any other clinical parameters like fatigue, blurring of

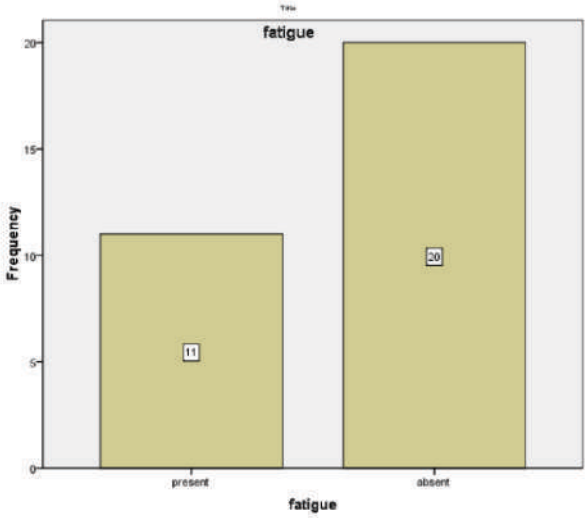
vision, fever, splenomegaly, dizziness or muscular weakness.

DISCUSSION

Multiple myeloma, as this study shows, commonly affects the elderly age groups of population and less commonly in the younger age group. In two studies,







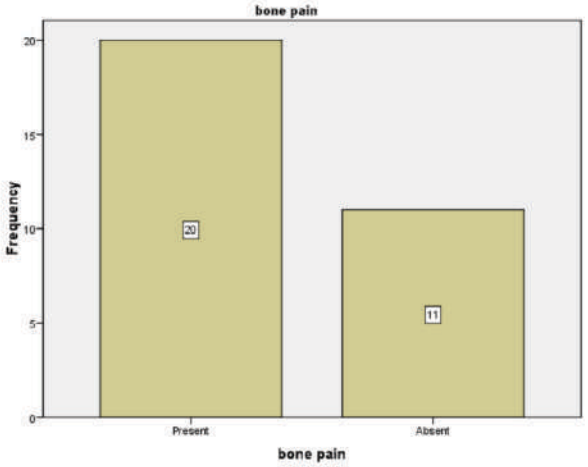


Table 2: Percentages of different signs and symptoms

	Symptoms/signs	Percentages
1	Bone pain	62%
2	Back ache	53%
3	Fatigue	34%
4	Dizziness	9%
5	Muscular weakness	12%
6	Pallor	81%
7	Headache	6%
8	Blurring of vision	6.3

Table 1: Laboratory parameters in patients(n-32)

	Hb (g/dl)	TLC ($x10^9$/l)	Platelets ($x10^9$/l)	MCV fl	ANC ($x10^9$/l)	Calcium (mg/l)	Creatinine (mg/l)	Albumin (g/l)	Plasma cells %
Mean	8.1	5.7	192.9	87.38	3.3	9.3	2.1	2.6	47
Standard deviation	1.5	2.7	108.6	7.24	2.2	1.5	1.8	.7	24.96
Minimum	4.7	1.10	20	61.2	.40	6.9	.3	1.2	3.6
Maximum	11.3	11.90	456	102.4	8.70	12.7	6.7	3.9	90

2% and 3.58% patients were less than 40 years respectively. We observed that there was only one patient younger than 40 years in our study while in another study of Sultan et al it was found in 13.1%[1]. The mean age of patients was 55.4, 51, 58.8 and 56 years in the studies of Wadhwa et al, Kaur et al and Sultan et al1,[4]. In our study, the mean age was 52.81 ± 9.36 years whereas in another study, it was 63 years. Bone pain (87.50%) and low backache (71.88%) were the commonly presented complaints. Sultan et al[18] observed fatigability in 81.9% and backache in 80.3% of the patients[1]. Kaur et al observed weakness and fatigability in 46.4% cases and bone pain in 50% cases[4]. Kyle et al[1] observed weakness and fatigability in 32% and bone pain in 58% cases[5]. In our observation, these percentages were found higher possibly because of the advanced stage at presentation. Pallor (81%) and bone tenderness (62%) were noted in our study.

Anemia in myeloma is caused due to replacement of marrow by myeloma cells and decreased production of erythropoietin due to accompanying renal involvement[3]. In some cases it may be associated with cytokine mediated bone marrow suppression. Hemoglobin value ≤ 10 gm/dL was seen in 63.9% of the patients in Sultan et al study and in the study of Wadhwa it was in 59% of the patients[1]. In the present study, hemoglobin less than 10g/dl was present in majority of patients (99%).

Thrombocytopenia may be due to infiltration of the marrow by plasma cells or intravascular destruction of platelets or thrombopoietic activity of IL-6. In our study thrombocytopenia was in 11(34%) cases, but in the study of Kaur et al[4] it was higher (25%) and in the studies of Diwan et al[22] and Kyle et al[5] it was in 10% and 5% of the patients respectively. In multiple myeloma, the main causes of renal failure are cast nephropathy due to light chain excretion and glomerular deposition of immunoglobulin. In the current study, raised serum creatinine was found in 22 % of the patients, which is similar to the findings in the study of Kaur et al[17] (86.4%), but it is higher than the studies of Kyle et al (55%) and Sultan et al[1,5] (40.9%). In our study serum creatinine was ≥2mg/ dL in 37% patients while in according to Kyle et al 19% have elevated serum creatinine.

Hypercalcemia remains the most frequent metabolic complication of myeloma patients and excessive osteolysis plays a major contributory role in its pathogenesis. In our study, mean calcium level was 9.3 mg/l. In a study by Kyle et al, 13% patients have hypercalcaemia but in a study by Sultan et al 47.5% have hypercalcaemia[1,5]. Low serum albumin is also a poor prognostic factor. In more than 90% of our patients serum albumin level was low, while in a study by Jacobson et al[6] it was in 20% of patients. It may be due to the reason that majority of our patients presented in later stages of disease.

CONCLUSION

In this study we were able to identify warning signs that may lead physicians to an early diagnosis of multiple myeloma ,which are back pain combined with other systemic symptoms such as fatigue and weight loss, or back pain combined with abnormal blood tests.

Limitations of Study

All investigations for different organ involvement and prognostic markers were not performed due to financial constraints. It is important to repeat this study in larger populations and in other clinical settings to determine whether there is justification for a guidance recommending early detection of multiple myeloma.

Conflict of Interests

There are no conflicts of interest to declare.

Contributions of Authors

Ahmad R: Analysed data and wrote manuscript

Arif F: Collected data and proof read manuscript

Khalid A: Proof read manuscript

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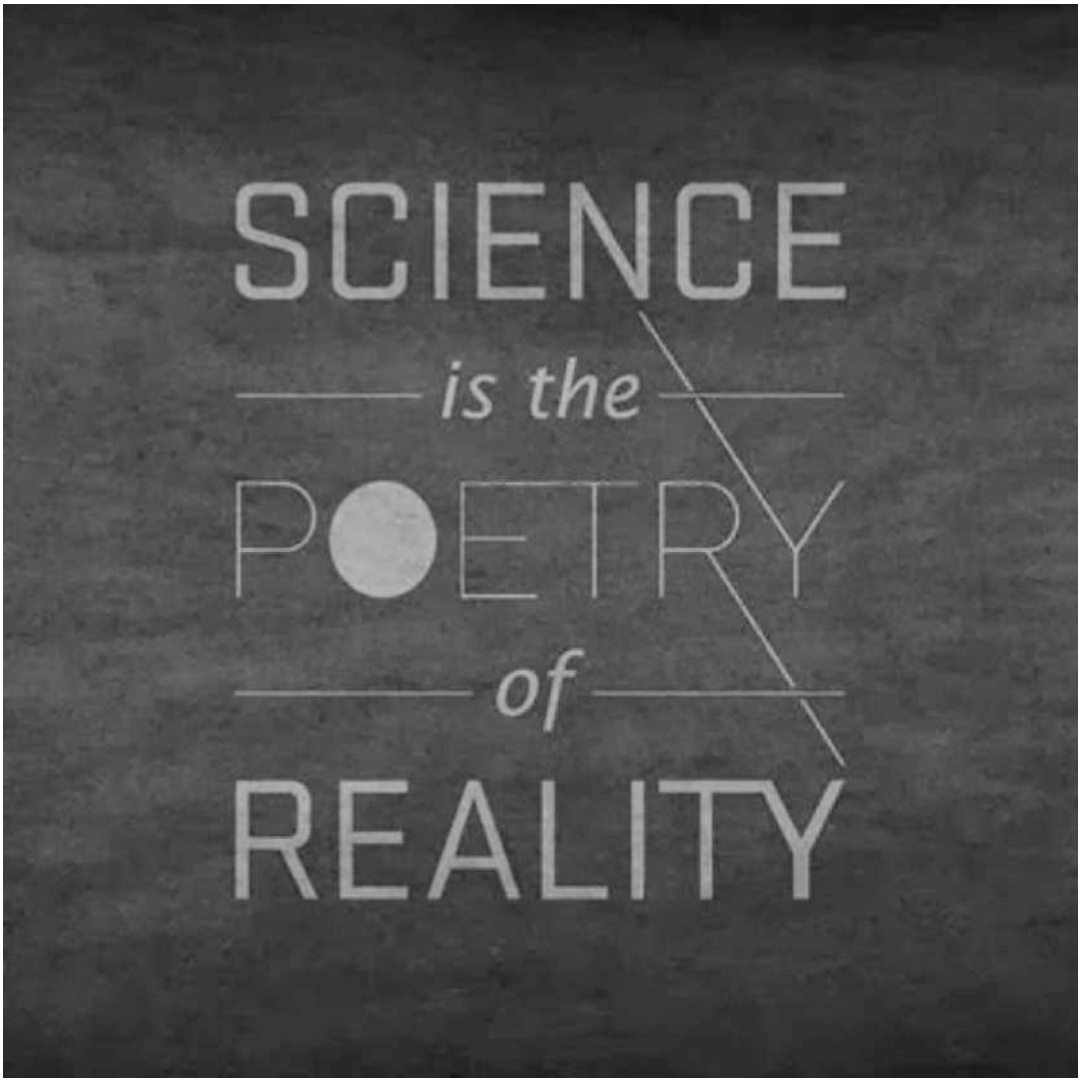

DIAGNOSTIC ACCURACY OF MAGNETIC RESONANCE IMAGING IN DIAGNOSIS OF ADENOMYOSIS

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Abstract

Background: The imaging diagnosis of adenomyosis is usually made by means of transvaginal ultrasonography (TVUS) or magnetic resonance imaging (MRI). Hysterosalpingography (HSG) and transabdominal ultrasonography (TAUS) often lack specificity for this diagnosis.

Objectives: To determine the diagnostic accuracy of Magnetic Resonance Imaging (MRI) in diagnosing adenomyosis taking histopathology as gold standard. It was a descriptive, Cross-sectional study was conducted at the Department of Radiology, Jinnah Hospital / Allama Iqbal Medical College, Lahore.

Methodology: A total of 200 patients with clinical symptoms like menorrhagia and dysmenorrhea for at least 12 months of age 30 to 55 years of female gender were included. Patients with history of fibroid disease and metallic prosthesis / metal implants (like cardiac pacemaker) were excluded. All the patients were then magnetic resonance imaging was performed in every patient using 1.5 Tesla MR System. MRI study was interpreted by consultant radiologist for diagnosis of uterine adenomyosis. Magnetic resonance imaging findings were compared with histopathology report.

Results: Mean age was 41.51 ± 10.77 years. Out of these 200 patients, 79 (39.50%) were primiparous and 121 (60.50%) were multiparous. In MRI positive patients, 114 were True Positive and 17 were False Positive. Among 69, MRI negative patients, 12 were False Negative whereas 57 were True Negative (p=0.602). Overall sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of MRI in diagnosing adenomyosis was 90.48%, 77.03%, 87.02%, 82.61% and 85.50% respectively.

Conclusion: This study concluded that magnetic resonance imaging (MRI) is the non-invasive modality of choice with high diagnostic accuracy in diagnosing adenomyosis.

Keywords: Adenomyosis, magnetic resonance imaging. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses).

Uterine adenomyosis is clinical condition of uterus in which there is invasion of myometrium by the endometrial glands and stroma.[1,2,21] Three subtypes are described, internal, external adenomyosis, and adenomyomas.[20] This condition in general affects women of reproductive age group in multiparous and with history of surgical uterine procedures (e.g. Caesarian section, dilatation and curettage). The patients of adenomyosis typically present with sign and symptoms of menorrhagia, dysmenorrhea and chronic pelvic pain. Some of patients may be asymptomatic. The prevalence of disease ranges from 8 to 27% in parous women with the final diagnosis made after hysterectomy.[3,21]

In adenomyosis, normal boundary between endometrial basal layer and myometrium is disrupted,

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as a consequence endometrial glands invade the myometrium, giving rise to ectopic intra-myometrium glands that cause hypertrophy and hyperplasia of adjacent myometrium.[3,4,5,6] Although it can be linked with endometriosis, but these are actually two different disease entities and may be found together in only 10% of the cases.[7]

Adenomyosis has a marked impact on women in reproductive age with increased risk of anemia.[3] Chronic lower abdominal pain & anemia can lead to fatigue, dizziness, and moodiness and symptoms like anxiety, depression, and irritability. Adenomyosis has association with an increased incidence of preterm labour & premature rupture of membranes.[3] So diagnosis of adenomyosis is very important.

As far as radiological imaging of adenomyosis is concerned, the diagnostic features of adenomyosis on ultrasound are unfortunately variable and may be absent some time. Sensitivity and specificity of transabdominal ultrasound are 32-63% and 95-97% respectively.[8] The primary test in the diagnosis of pelvic endometriosis and adenomyosis is transvaginal ultrasonography. The sonographic differential diagnosis of focal adenomyosis includes uterine fibroid.[19]

PRISMA statement recommends, transvaginal sonography (TVS) and magnetic resonance imaging (MRI) as modality of choice for diagnosis of adenomyosis.[(20)]

MRI as a non-invasive technique with increased soft tissue differentiation, allowable higher spatial & contrast resolution provides better diagnostic capability for adenomyosis. MRI is the imaging gold standard for diagnosing adenomyosis, however its access is often limited with high costs and availability.[22] MRI has ability to differentiate adenomyosis from multiple small uterine fibroids[9] which may also present with similar symptoms. So with magnetic resonance imaging (MRI), adenomyosis can be diagnosed pre-operatively with increasing frequency in parous women.[9,20] A study reported MRI quite accurate in diagnosing adenomyosis (area under curve 0.91).[4] In a study, the sensitivity and specificity for the diagnostic accuracy of MRI in this context were reported 74% and 91% respectively.[6] But another study concluded that in the diagnosis of adenomyosis, MRI had sensitivity of 46.1%, specificity of 99.1%, PPV of 92.3%, and NPV of 88.5%. The area under the curve (AUC) for the diagnostic performance of MRI in the detection of adenomyosis was 0.73.[5]

The available studies are controversial regarding the utility and accuracy of magnetic resonance imaging. This study would help us determine the potential use of MRI for the diagnosis of adenomyosis. If accuracy came out low, we may delineate guidelines to discourage its use or vice versa. Moreover, as the disease frequency was expected to be changed over time so positive predictive value was also expected to be changed, also there was no local literature available, for early diagnosis and treatment our study will add a non-invasive technique to reduce unnecessary diagnostic biopsies / radical surgeries in adenomyosis which would decrease complication rates of such diagnostic and therapeutic interventions.

METHODOLOGY

This study was Descriptive, Cross-sectional carried out at department of Radiology Jinnah Hospital / Allama Iqbal Medical College Lahore from March 2020 to December 2020. SAMPLE SIZE: Estimated sample size is 200 patients, taking confidence interval 95%, at 91% specificity, 46% sensitivity and 27% prevalence of Uterine adenomyosis,[5] with 12 % margin of error for sensitivity and 5 % margin of error for specificity of MRI in diagnosing adenomyosis, taking histopathology as gold standard. Sample Technique: Non-probability, consecutive samp-ling. Sample Selection: a. Inclusion Criteria: Female gender. Age 30 – 55 years. Patients with clinical symptoms like menorrhagia and dys-menorrhea for at least 12 months and advised hyste-rectomy by a consultant gynecologist. Menorrhagia was labelled as heavy menstrual bleeding (> 80 ml blood loss in a cycle) assessed by measuring the difference between dry and soaked pads where 1 gram = 1ml. b. Exclusion Criteria: Age <30 years or >55 years. Or Claustrophobic patients. History of fibroid disease

determined by clinical record (i.e., previous Ultrasound/ CT/ MRI). Patients with metallic prosthesis / metal implants (like cardiac pacemaker, etc).

After informed consent and taking approval from departmental ethics committee, 200 patients according to selection criteria presenting to department of gynecology were included in study. Included patient had magnetic resonance imaging of pelvis with 1.5 Tesla MR unit (Philips) performing high resolution 4mm thickness slices multiplaner images, T1. T2 weighted spin echo and gradient echo images were obtained with and without fat saturation. Consultant radiologist with 5 years post fellowship experience reported the MRI for diagnosis of uterine adenomyosis without prior knowledge of biopsy results. After hysterectomy, patient was followed for the biopsy report from the department of pathology, Allama Iqbal medical college, Lahore. Data was collected on structured proforma containing background information i.e. age and diagnosis of adenomyosis on both histopathology and MRI. Researcher himself recorded data according to operational definitions.

Data collected was entered and analyzed in the SPSS version 22. Mean with standard deviation were calculated for quantitative variables like age, and frequency and percentage in case of categorical variables like presence of uterine adenomyosis. A 2 × 2 table was generated and sensitivity, specificity and accuracy were labeled (Figure-1). Data was stratified for age groups, BMI, parity and previous C-sections. Chi square test was used post stratification. A p value < 0.05 was considered significant (Table-1).

RESULTS

Age range in this study was from 30 to 55 years with mean age of 41.51 ± 10.77 years. Majority of the patients 66 (33.0%) were between 30 to 40 years of age.

Out of these 200 patients, 79 (39.50%) were primiparous and 121 (60.50%) were multiparous. Mean BMI was 32.18 ± 3.45 kg/m^2.

All the patients were subjected to magnetic resonance imaging (MRI). MRI supported the diagnosis of adenomyosis in 131 (65.50%) patients. Histopathology findings confirmed adenomyosis in 126 (63.0%) cases. In MRI positive patients, 114 were True Positive and 17 were False Positive. Among 69, MRI negative patients, 12 were False Negative whereas 57 were True Negative (p=0.602).

Overall sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of MRI in diagnosing adenomyosis was 90.48%, 77.03%, 87.02%, 82.61% and 85.50% respectively.

Table 1: *Summary of Results.*

	Positive result on MRI	Negative result on MRI	P-value
Positive on Histopathology	114 **(TP)***	12 **(FN)*****	**0.602**
Negative on Histopathology	17 **(FP)****	57 **(TN)******	

*-TP=True positive **-FP=False positive ***-FN=False negative ****-TN=True negative

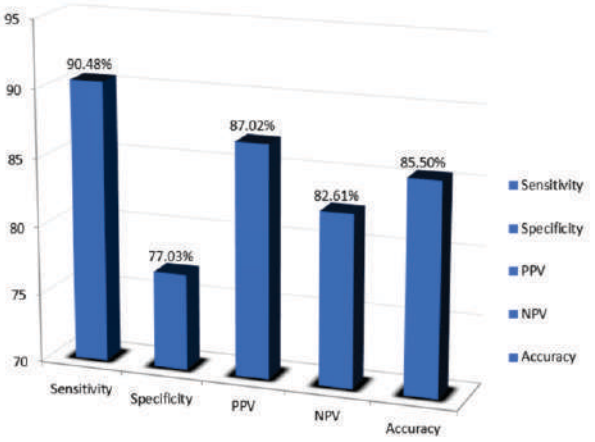

Figure-1: *Diagnostic Accuracy of MRI in Diagnosing Adenomyosis, taking Histopathology as Gold Standard.*

DISCUSSION

Uterine adenomyosis is a common gynaecological disorder. It is a disease of multiparous women in fourth and fifth decades of life. The reported incidence of adenomyosis in unselected hysterectomy specimens

ranges from 8.8% to 31%.[10] Transvaginal Ultrasound & MRI (Magnetic Resonance Imaging) are usual modalities for the diagnosis of adenomyosis. Hysterosalpingography (HSG) and transabdominal ultrasonography (TAUS) often lack specificity for this diagnosis. Computed Tomography (CT), due to its inability to resolve subtle differences in soft-tissue attenuation limits its usefulness in diagnosing adenomyosis. Hormonal stimulation & Treatment can change MRI appearance of adenomyosis. Rarely, endometrial carcinoma can arise from adenomyosis. T2-weighted & contrast enhanced T1-weighted images improves the accuracy of staging in cases of adenomyosis coexisting with endometrial carcinoma.[11-12]

In this study age ranges from 30 to 55 years with mean age of 41.51 ± 10.77 years. Majority of the patients 66 (33.0%) were between 30 to 40 years of age. All underwent magnetic resonance imaging (MRI). Adenomyosis was diagnosed in 131(65.50%) patients on MRI. Histopathology confirmed adenomyosis in 126 (63.0%) patients. In MRI positive patients, 114 were True Positive and 17 were False Positive. Among 69, MRI negative patients, 12 were False Negative whereas 57 were True Negative (p=0.602). Overall sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of MRI in diagnosing adenomyosis was 90.48%, 77.03%, 87.02%, 82.61% and 85.50% respectively. In one study, MRI accurately diagnosed adenomyosis (area under curve 0.91).[4] In another study, the sensitivity and specificity for the diagnostic accuracy of MRI in this context were reported 74% and 91% respectively.[6] But another study concluded that in the diagnosis of adenomyosis, MRI had sensitivity of 46.1%, specificity of 99.1%, PPV of 92.3%, and NPV of 88.5%. The area under the curve (AUC) for the diagnostic performance of MRI in the detection of adenomyosis was 0.73.[5]

Comparing ultrasound and MRI for the diagnosis of adenomyosis, Bazot et al. (2001) found no difference in accuracy in diagnosing adenomyosis between transvaginal ultrasound and MRI, but sensitivity was significantly lower with ultrasound in patients with associated Fibroids. They reported sensitivity, specificity, and positive and negative predictive values for transvaginal ultrasound and MRI of 76.4% and 92.8%, and 73.4% and 88.8%, 77.5% and 92.5%, and 83.8% and 89.2% respectively. However, sensitivity and specificity of transvaginal ultrasound for the diagnosis of adenomyosis in patients with and without leiomyomatosis were respectively 33.3% and 78%, and 97.8% and 97.1% whilst for MRI these figures were 66.6% and 82.1%, and 86.7% and 100%.[13]

In a retrospective review on 1517 women, the MRI and pathology report were the same for 136 of 144 women with leiomyoma and 12 of 31 women with adenomyosis. The MRI had 94% sensitivity and 33% specificity for leiomyoma and 38% sensitivity and 91% specificity for adenomyosis. Positive and negative predictive values of MRI for leiomyoma were 95% and 27% with 90% accuracy. Positive and negative predictive values of MRI for adenomyosis were 52% and 85%, respectively, with 80% accuracy.[14]

Some studies evaluating MRI performance for the diagnosis of adenomyosis show a sensitivity of 70% to 86% and a specificity of 86–93%, with a mean accuracy of 87.5%.[13,15,16] These numbers were similar for the diagnosis of adenomyosis on ultrasound.[13,16] Therefore opinion is divided about the diagnostic test of choice. The advantage of MRI is less interoperator variability and also permits a more specific diagnosis. The presence of Uterine leiomyomas in almost 50% of patients with adenomyosis, causes ultrasound analysis more difficult and less efficient.[13,17] In these situations, the recourse to MRI is useful especially when conservative treatment has been chosen. MRI however has certain limitations.

MRI has limitations for the evaluation of a fundamental indirect sign: the thickness of the junctional zone. The junctional zone thickness is not measureable in 20 to 30 % during their reproductive cycle and this percentage increases to 50% in postmenopausal women.[13,17] In some patients, the junctional zone is not visible and in others it may not be distinguishable from the outer myometrium; finally, the presence of myomas can render the junctional zone measurement

difficult if not impossible. Reinhold et al[15] did not identify any patient with adenomyosis and a non-measurable junctional zone. However, Bazot and colleagues[13] reported 22% of patients having proven adenomyosis and a non-measurable junctional zone. In one study, investigators evaluated several different types of T2-weighted sequences: true fast imaging with steady-state free precession, turbo inversion recovery, and turbo spin-echo T2.[18] They found that sequences performed with breath-holding improved the ability to determine the thickness of the junctional zone and reduced inter-observer variability.[18] On the whole it is concluded that magnetic resonance imaging (MRI) is the non-invasive modality of choice with high diagnostic accuracy in diagnosing adenomyosis, and has not only dramatically improved our ability of accurate diagnosis of adenomyosis pre-operatively but also helps the surgeons for proper decision making.

CONCLUSION

This study concluded that magnetic resonance imaging (MRI) is the non-invasive modality of choice with high diagnostic accuracy in diagnosing adenomyosis, and has not only dramatically improved our ability of accurate diagnosis of adenomyosis pre-operatively but also helps the surgeons for proper decision making. So, we recommend that magnetic resonance imaging (MRI) should be done routinely in all cases of adenomyosis for accurate assessment pre-operatively and opting proper surgical approach and reducing pure diagnostic biopsies which ultimately reduce the morbidity and mortality of these patients.

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Conflict of Interest None

Ethical Issue According to the authors there is no ethical issue in this study.

Authors Contributions

Conception & Design Dr. Adnan Ahmad Sattar, Dr. Naeem Ahmad Khan, Dr. Tanweer Ahmad.

Collection & Assembly of data Dr. Shehzad Masood, Dr. Adnan Ahmad Sattar, Dr. Kamran Ahmad Dodhy.

Literature Review & Critical Revision of the article for important intellectual content Dr. Adnan Ahmad Sattar, Dr. Naeem Ahmad Khan, Dr. Tanweer Ahmad, Dr. Kamran Ahmad Dodhy, Dr. Basma Khan.

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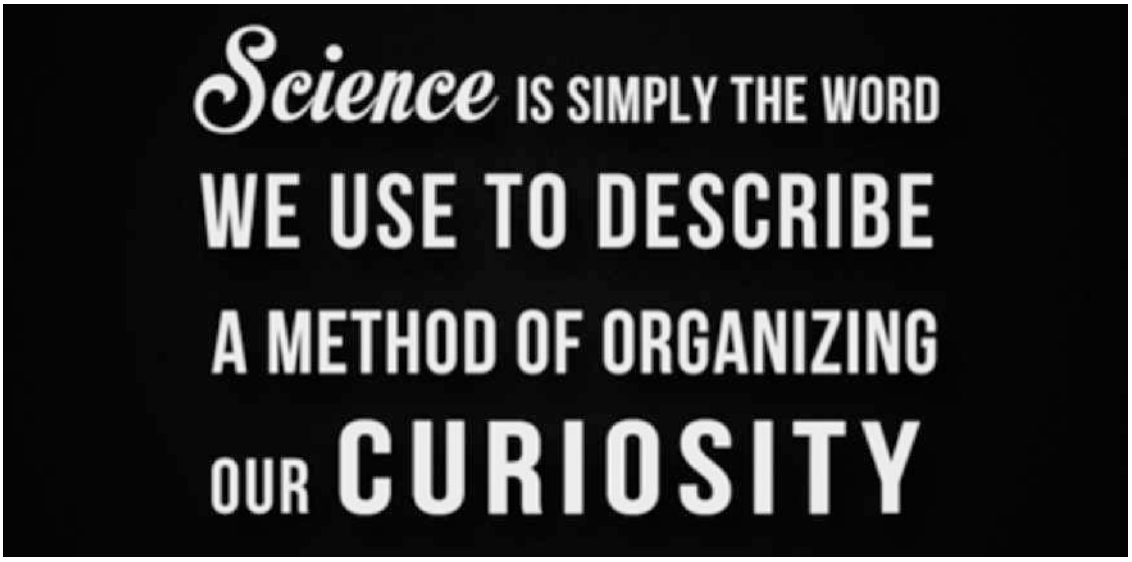

INCIDENCE OF THYROID CARCINOMA IN MULTINODULAR GOITER: A HISTOPATHOLOGICAL SCRUTINY OF 148 CASES

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Abstract

Background: All over the world, prevalence of multinodular goiter and its association with incidental thyroid cancers varies considerably.

Objective: The intention of this study is to assess the incidence of thyroid malignancy in patients subjected to thyroidectomy due to multinodular goiter.

Methodology: Histopathological examination was done on 148 thyroidectomy specimen removed due to multinodular goiter to ascertain the presence of incidental thyroid carcinomas.

Results: 12 (8.1%) out of 148 thyroidectomy specimen removed due to multinodular goiter were found to have incidental carcinomas on histopathological analysis. Papillary carcinoma was the most frequently noticed malignant tumor.

Conclusion: The probability of having malignancy in multinodular goiter is always there and should not be ignored; while assessing these patients, thorough preoperative work up must be done along with post op histopathological analysis.

Key Words: Thyroid, carcinoma, multinodular goiter.

Thyroid enlargement in the form of multinodular goiter is the most frequent clinical presentation of a vast variety of thyroid diseases.[1] The utmost apprehension in these individuals is to exclude the chance of having any sort of malignancy. The frequency of thyroid malignancy fluctuates in various regions of the world. In the past it is considered unusual to find thyroid malignancy in patients presenting with multiple nodules; though the latest surveys reveal the frequency up to 35%. [2,3]

Sadly, the prevalence of thyroid related malignancies especially in multinodular goiter is hard to evaluate in Pakistan because of scarcity of population based researches and here people hardly go for surgery until and unless they start having compression symptoms. Still various studies reflect comparative increase in their incidence.[1,4]

Thyroid diseases are frequently encountered in clinical practice. A large majority of these disorders are of benign category.[5] Previously they are considered frequent mainly in mountainous hilly regions deficient in iodine.[1,5,6] But these nodules are commonly found even in iodine sufficient regions especially during ultrasonography neck.[2,7]

Long standing multinodular goiter is linked with a substantial rate of incidental thyroid carcinoma and is counted as one of the predisposing factor of thyroid malignancy which should not be ignored and must be evaluated histopathologically after removal from body.[8]

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The objective of this study is to determine the prevalence of incidental carcinomas in patients undergoing thyroidectomy for multinodular goiter.

METHODOLOGY

This descriptive study is conducted at histopathology department of Bakhtawar Amin Hospital, Multan over a period of almost two years from Jan 2019 to March 2021. Every thyroidectomy specimen with clinical and histopathological impression of multinodular goiter was included in this study. Patient's demographic particulars, relevant radiological investigations, gross details and microscopic diagnosis of the excised thyroid specimen were noted from the patient's case folders, histopathology registers, operation documentations and laboratory request forms. Cases with inadequate data, Grave's disease, solitary thyroid nodule, thyroiditis, known cases of carcinomas and lymphadenopathy were excluded from the study.

The hematoxylin and eosin (H&E) stained slides were viewed. The data was noted on a predesigned excel sheet. Percentage and means were calculated. Relevant tables and charts were computed.

RESULTS

A total of 148 thyroidectomy specimens due to multinodular goiter were received in histopathology department of Bakhtawar Amin Hospital, Multan. Out of these, 12(8.1 %) cases appeared malignant on histopathological examination. Papillary carcinoma was the most frequently encountered incidental tumor in our study. Number and percentage of males and females were 3 (25 %) and 9 (75 %) respectively. The mean age was 45 years (ranging from 28-79 years). In two malignant cases, subtotal thyroidectomy was performed; in all other malignant cases, total thyroidectomy was done.

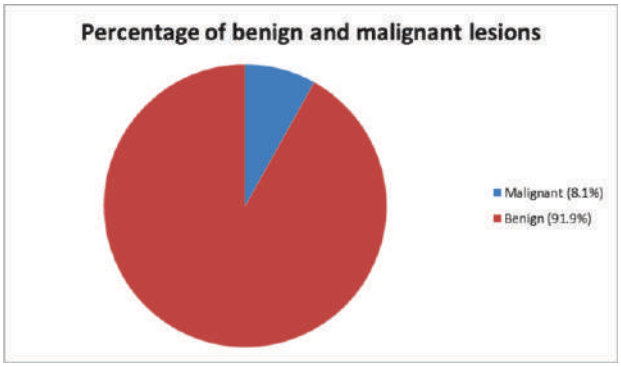
Table 1: *Types, Number and Percentage of Malignancies Found in this Study*

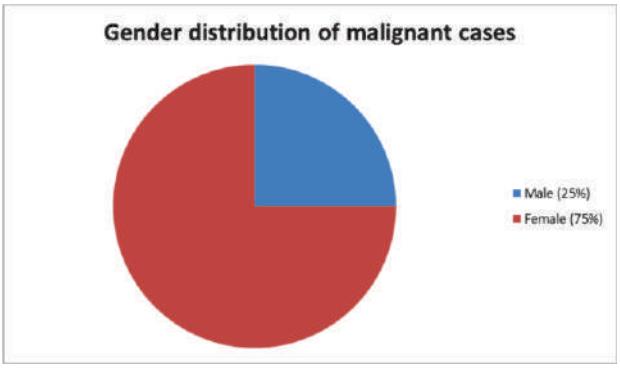
Type of thyroid carcinoma	Number of cases	Percentage (%)
Papillary Carcinoma	09	75
Follicular Carcinoma	02	16.7
Anaplastic Carcinoma	01	8.3

Table 2: *Number & Percentage According to Thyroidectomy Types*

Type of Thyroidectomy	Number of cases	Percentage of cases (%)
Total Thyroidectomy	111	75
Subtotal Thyroidectomy	28	18.9
Near total Thyroidectomy	09	6.1

Distribution of malignant and benign lesions on histopathological analysis of this study (Percentage)





Gender distribution of malignant cases (Percentage)

DISCUSSION

Multinodular goiter is the most frequent disease of thyroid gland[9] and forms a major bulk of endocrine disorders exerting influence on millions of people globally; esp. in developing nations.[10]

Several studies conducted in Pakistan reveal frightening prevalence of multinodular goiter in various regions;[11,12] and also disclose that a high proportion of cases of thyroid malignancy in Pakistan present as multinodular goiter instead of solitary thyroid nodules.[13]

Even the studies that figured higher frequency of cancers in solitary thyroid nodules stated much higher frequency of thyroid malignant neoplasms in multinodular goiter.[14]

The frequency of thyroid malignancy has been expanded worldwide up to five times in last half century;[15,16] especially the incidental finding of thyroid carcinoma in multinodular goiter. The cause(s) for this global rise are yet ill defined. Several factors are considered among which the enhanced diagnostic procedures and immense evaluation grasp the most attention.[17]

In the present study, we found 12 (8.1%) cases of thyroid carcinomas out of 148 multinodular goiter specimens on histopathology. This was in accordance with the studies conducted by Ghadban BR, Imad et al and Bombil I; where they found 10%, 11.2% and 5.7% incidence of malignancy in multinodular goiter.[1,10,18]

Papillary carcinoma was the most frequent cancer found in our study. This was in accordance with many other studies conducted in various countries where papillary carcinoma of thyroid appears to be the major proportion of overall thyroid malignancies; however, there is marked variation of percentage rise between states.[19,20]

According to study by Imad S et al the incidence of papillary carcinoma was 66.6%, comparable to 75% in our study.[1]

The gender distribution of malignant cases in our study was 25% males and 75% females almost equivalent to study by Shrestha D (28%/72%). [(21)]

The mean age in our study was 45 years (ranging from 28-79 years) approximately equal to the studies conducted by SG Terzioğlu et al, Ghadhban BR and I Bombil where they found mean ages, 48.69, 43.9 and 46 years respectively.[22,10,18]

CONCLUSION

The probability of having thyroid malignancy in patients with multinodular goiter is no less than those with solitary nodules and while assessing these patients, thorough work up must be done before proceeding for surgery to spot any malignant focus and total thyroidectomy by surgical experts should be opted in patients with multinodular goiter particularly in men and adolescents.

Limitations of Study

Many patients are non-affording and hardly go for expensive investigations like thyroid scan or even ultrasound neck. This could be the reason of missing small malignant foci. The study should be done on large scale to cover maximum number of population for confirmation of our findings.

Disclaimer

The abstract has not been previously presented or published in any conference, not a part of any research, PhD or thesis project.

Conflict of Interest None

Funding Source None

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CHANGING TRENDS OF DRUG ADDICTION IN YOUNGS

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Abstract

Background: One of the oldest curses is addiction. Humans have used various substances in different eras for getting pleasure. The oldest being smoking, pan, cannabinol & in late centuries mostly alcohol & sheesha with the changing ages the mode & materials for this purpose from simple tobacco to newer drugs. The term drug has now been given a new connotations. Drug addiction in any form is a known health hazard being responsible for many systemic diseases.

Objectives: To determine the changing trends of drug addiction among youths

Methodology: A total of 150 youngs both male and female participated in the study selected through Non-Probability Convenient Sampling technique. A questionnaire includes both open ended & close ended questions regarding knowledge about different types of addictive drugs, their harmful effects and reasons for consuming these drugs.

Results: This study has been conducted through a survey among known addicts between the age of 15-35 years, among which are 93 males and 57 females .The result shows that males are more involved than females .Middle class is more involved than upper and lower class. Duration of intake of drugs is 1-2 years in 68 people (both male and female) and these addicts are associated with life threatening diseases (more commonly hepatitis).Addiction is common in students and employees. Frequency of started drug is cigarette smoking in every class of individuals and then they most commonly switch to alcohol, hashish and shisha.

Conclusion: Prevalence of drugs addiction with changing ages the mode and materials for this purpose have also changed from simple tobacco smoking to sophisticated drugs.

Key Words: Drug Addiction, Sheesha, Charas, Naswar, Convenient Sampling

One of the oldest curses is addiction. Humans have used various substances in different eras for getting pleasure. The oldest being smoking, pan, cannabinol & in late centuries mostly alcohol & sheesha with the changing ages the mode & materials for this purpose from simple tobacco to newer drugs. The term drug has now been given a new connotations.[1]

Drug addiction in any form is a known health hazard being responsible for many systemic diseases. Young students initially start cigarette smoking & end up using alcohol, weed, sheesha, ice crystal, cracks, without realizing physical & mental damage.[2]

Most vulnerable age group for becoming addict to this misfortune was 15-35 years age. Our study reveals that friends were the main source for offering these drugs for the first time. The addicts become dependent on the drugs & use it despite full knowledge.[3]

UNODC estimates 155-255 million populations which is 3.5-5.7 % of world population between the age of 15-64 used illicit drugs top along with alcohol & tobacco.[4]

Causes of drug addiction include job frustration, lack of interest in education, neglect of parents, increased availability in low prices, rapidly changing social norms, influence of friends, social & family stress, other family members involved in drugs, broken affairs & easy availability of drug without prescription.

QURAN says in Surah Nisa, verse 29 “don’t kill yourself” & Prophet (SAWW) says in explanation to this verse “whoever kills himself with poison than

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his poison will be in his hand & he will keep taking it in the fire of Jahanum forever & ever" (Tafseeribn e Kaseer). It is a clear lesson. For us that every Muslim should abstain from addiction of every sort. Because it is totally prohibited in the religion. But on the contrary it is observed that our youth is converting to more sophisticated form of addiction like ice crystal, heroine, charas, guttuka from simple pan & tobacco.[5]

METHODOLOGY

This study was conducted in two universities at Iqra University Islamabad & one at Ameer ud Din Medical Collage Lahore. This study was conducted from December, 2019 to January, 2020.

It was a descriptive cross sectional study

Total 150 students both male & female from each university of age 16-35 years were selected by convenience sampling. The participants were informed about study objectives before data collection. Questionnaire were filled in only by those who agreed to participate in the present study. All data were anonymized. Undergraduate students were included who agreed about drug abuse history & those are excluded who disagreed to do drug abuse. Data was entered & analyzed on SPSS (Statistical Package for the Social Sciences) version 16.

RESULTS

This study has been conducted through a survey among known addicts between the age of 15-35 years, among which are 93 males and 57 females .The result shows that males are more involved than females .Middle class is more involved than upper and lower class .Duration of intake of drugs is 1-2 years in 68 people (both male and female) and these addicts are associated with life threatening diseases (more commonly hepatitis).Addiction is common in students and employees. Frequency of started drug is cigarette smoking in every class of individuals and then they most commonly switch to alcohol, hashish and shisha.

DISCUSSION

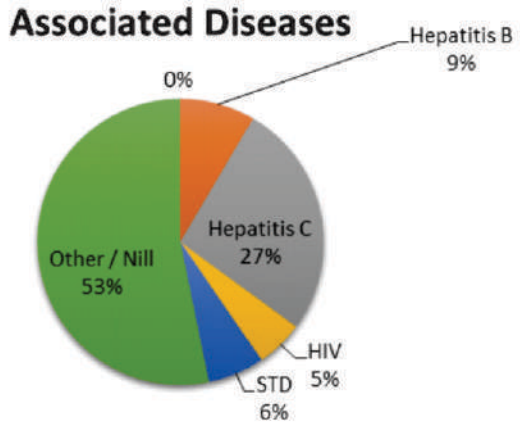
The current study about changing trends of drug abuse utilizing a questionnaire shows that addiction is changing rapidly from simple tobacco to sheesha, from cannabis to morphine, alcohol to ice crystal and other sophisticated drugs. This trend is quite dange-

Duration of Intake

Sr. No.	Duration	Total Cases	Male Cases	%age	Female Cases	%age
1	Less Than 1 Year	30	21	14.0	9	6.0
2	1 - 2 Years	68	40	26.7	28	18.7
3	5 - 10 Years	36	19	12.7	17	11.3
4	More than 10 Years	16	13	8.7	3	2.0
Total		**150**	**93**	**62.0**	**57**	**38.0**

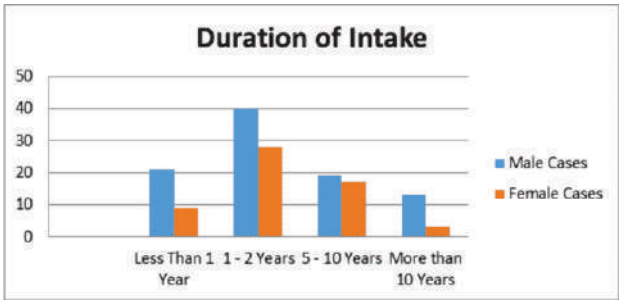
Income Status

Sr. No.	Duration	Total Cases	Male Cases	%age	Female Cases	%age
1	**Poor**	25	15	10.0	10	6.7
2	**Middle**	66	41	27.3	25	16.7
3	**Upper**	59	37	24.7	22	14.7
Total		**150**	**93**	**62.0**	**57**	**38.0**



Status of Narcotics

Sr. No.	Narcotis	No. of Cases	%age	Switch Drugs	No. of Cases	%age
1	Smoking	86	57.3	Smoking	16	10.7
2	Naswar	14	9.3	Pills	11	7.3
3	Crystal Ice	4	2.7	Crystal Ice	6	4.0
4	Alcohol	12	8.0	Pan-Gutka	7	4.7
5	Hashish	10	6.7	Charas	7	4.7
6	Pan	6	4.0	Naswar	16	10.7
7	Charas	6	4.0	Hashish	18	12.0
8	Pills	6	4.0	Alcohol	23	15.3
9	Gaunja	1	0.7	Weed	3	2.0
10	Sedatives	3	2.0	Shisha	33	22.0
11	weed	2	1.3	Morphine	4	2.7
Total		**150**	**100.0**	Heroine	2	1.3
				Cocaine	4	2.7
				Total	**150**	**100.0**



rous and youth particularly is getting affected.[5] The rescue is minimum and is not being addressed in our society at micro as well as macro level.

Our institutes are now a hub for drug addiction and teacher is a central element in the educational system and plays a exclusive role in the classroom in reducing or counselling about drugs abuse where different kinds of students including aggressive, polite, slow learner, problematic, active etc are present.[6] Teachers can bring all these students under his/her umbrella of loyalty to make them well reputed citizen of country.[7]

Due to cumerbusan situation in education, jobs and family matters the condition of drug addiction has become worse. Moreover, negative impact of media as shown in dramas and films and moreover our social taboos like not to discuss things with our kids on these topics in poor society and not to ask anything in our rich society, these trends has brought this thing to the level of worry.[8]

Worldwide, annual rate of 4.9 million deaths have been reported due to tobacco abuse and this rate might rise to the 10 million in the next 20 to 30 years. 70% of these deaths takes place in developing countries and Pakistan is one of them.[9]

The approach and availability of drugs is not difficult for drug abusers despite being illegal. The use of these drugs causes dependency which leads to adoption of unusual means and crimes like stealing, robbery, fraud, and burglary, also seen in our society.

CONCLUSION

This study reveals the changing trends of drug addiction in youngs. Prevalence of drugs addiction with changing ages the mode and materials for this purpose have also changed from simple tobacco smoking to sophisticated drugs.

Limitation of the Study

This study is limited within the youngs of the Punjab province.

Acknowledgment

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Conflicts of Interests

There is no conflicts of interest with any person, institute or agency regarding publication of this manuscript.

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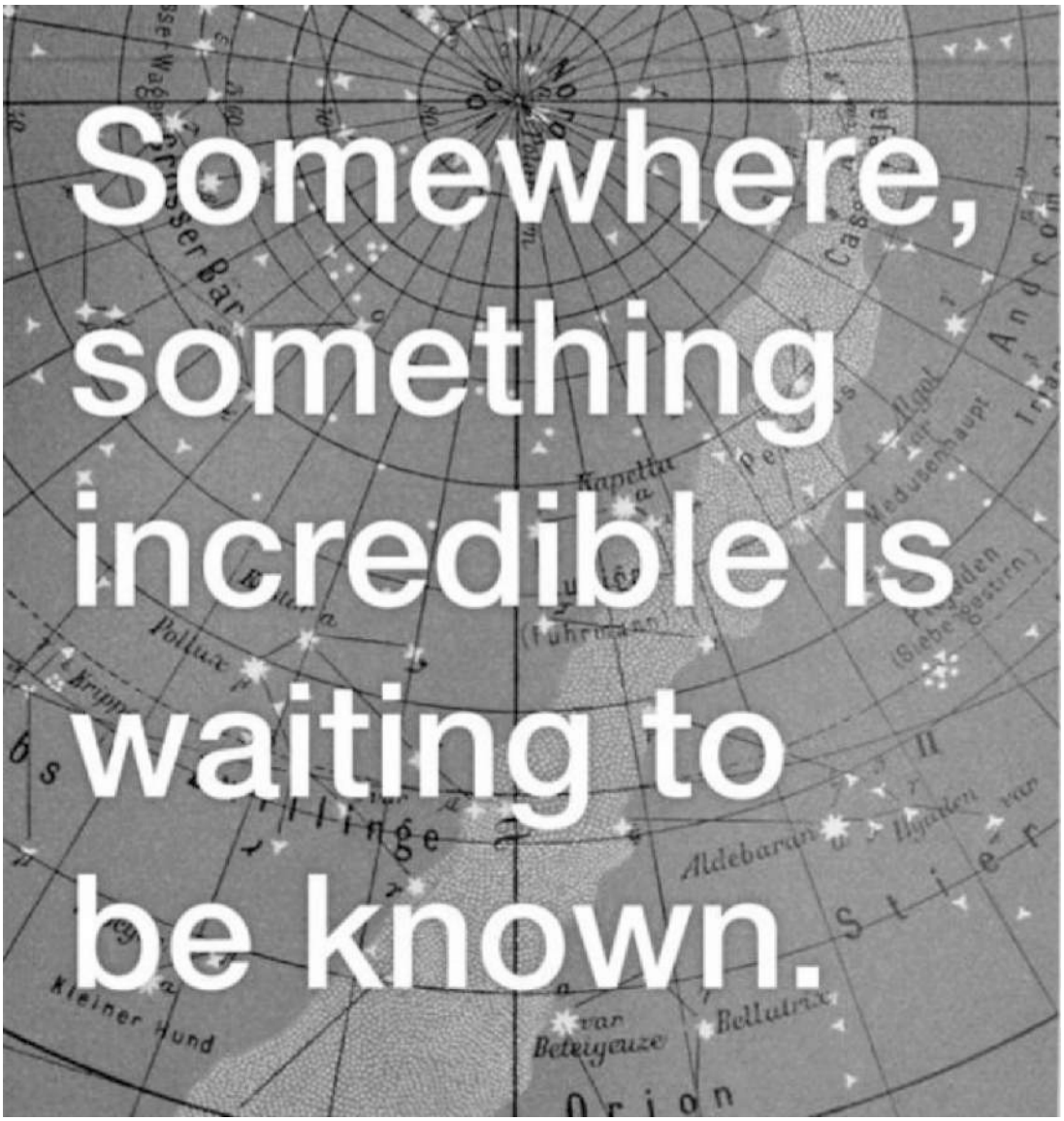

THYROID STIMULATING HORMONE, A BASELINE INVESTIGATION IN MANAGING INFERTILITY

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Abstract

Objective: To determine the prevalence of hypothyroidism in infertile women using TSH as the diagnostic screening tool. It was a cross sectional study.

Methodology: This study was conducted in a private clinic with good infertility gynecological practice. A total of 1516 , from January 2017 to February 2020, subfertile patients visiting our infertility clinic were investigated for thyroid stimulating hormones (TSH). Hypothyroidism was considered for TSH greater than 4.0.

Results: A total of 243 patients were hypothyroid, giving a high percentage of 16% prevalence of hypothyroidism in infertile women.

Conclusion: TSH of all infertile patients should be checked as a base line investigation at the first visit of infertility evaluation before going for expensive and invasive procedures.

Keywords: Hypothyroidism. Infertility, TSH

The failure to achieve a clinical pregnancy after 12 months or more of regular unprotected sexual intercourse[1] is defined as infertility.[2] Infertility is a world health issue. The prevalence of infertility may vary considerably according to the ethnic background[3] Infertility rates differ between countries ranging from 5 to 8 % in developed countries and from 5.8 to 44.2% in developing countries.[4] Thyroid disorders are the most common endocrinological disorders met within infertile women. The prevalence of thyroid disorders are 3 to 4 times higher in women than men.[5] Thyroid hormone receptors are abundantly present throughout the human female reproductive tract, including in granulose cells and oocytes.[6] Normal thyroid functions are necessary for fertility, pregnancy, and to sustain a healthy pregnancy especially in the earliest days of conception.

Thyroid disorders may appear as hyperthyroidism or hypothyroidism. Hypothyroidism is a common disorder in the general population. It is characterized by diminished metabolism, retarded growth and development, impaired mental activity and swelling of certain parts of skin. It has been reported that hypothyroidism has adverse effects on female reproduction, including a decreased chance of ovulation due to menstrual irregularity, miscarriage and preterm labour[6]. Thyroid disorders may not only effect menstrual cycle but play a pivotal role in delayed puberty and infertility, by resulting in anovulatory cycles, leuteal phase defect, high prolactin levels and sex hormone imbalance.[7] Hypothyroidism decreases the clearance of androstenedione and estrone, whereas peripheral aromatization is increased. In addition, the plasma binding activity of SHBG is decreased. Consequently, plasma concentration of both total testosterone and E2 are decreased and their unbound fraction increased.[8]

Thyroid evaluation is mostly done in women

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with family history of thyroid problems, irregular menstrual cycles, and recurring miscarriage. In Pakistan prevalence of hypothyroidism is 4.1%. Women are more likely to develop hypothyroidism than men, with the difference being significant after 34 years of age.[9] Thyroid evaluation in our set up is done by T3 T4 and TSH. It is a disease caused by lack of iodine in drinking water. In case of sufficient iodine intake, autoimmune thyroid disease Hashimoto thyroiditis appears to be the most common cause. In this case the healthy thyroid tissue due to prolonged inflammation is replaced by lymphocytic and rubbery tissue.[9] Rates of infertility have been reported to approach 50% in women with Hashimoto thyroiditis and Graves' disease.[10] Hypothyroidism is a clinical condition due to deficiency of thyroid hormone and raised level of TSH. Thyroid disorders may appear as subclinical or clinical hypothyroidism. Subclinical hypothyroidism (SH) is defined as an abnormally high thyroid stimulating hormone.[11] TSH level with a normal free thyroxine (FT4), and without frank symptoms of hypothyroidism. Thyroid prevalence of subclinical hypothyroidism is considered to be 2-10 %in general population and 0.9 to 40% in women of reproductive age.[9] Subclinical hypothyroidism is much more prevalent then clinical hypothyroidism. There are other causes of hypothyroidism, like subtotal or total thyoidectomy, interferone therapy, etc. but previously two mentioned are more significant in healthy infertile couples. It has also been observed by studies that women with hypothyroidism conceived with ART had a significantly increased risk of any congenital malformation.[12]

Population Based Infertility Data of women with subclinical and clinical hypothyroidism in our region is lacking. So we decided to conduct a study on it. TSH is a 28-Da glycoprotein released from thyrotrophs in the antromedial[13] region of the pituitary gland that stimulates thyroidal thyroxin T4 and triiodothyronine T3. There is a strong inverse relationship between serum TSH and free T4 concentrations. Small changes in T4 will provoke very large changes in serum TSH. The diagnostic superiority of TSH measurement arises principally from this inverse log/linear relationship between circulating TSH and free T4 concentrations. Serum TSH concentrations are considered the most reliable indicator of thyroid function abnormalities, and TSH analysis stands as the primary means of studying thyroid functions.[14]

Some Researchers have reported that only elevated TSH, not free thyroxin level, was associated with adverse pregnancy outcomes indicating that serum TSH level is a potent index for female reproduction issues.[15] So we selected TSH as the tool to detect hypothyroidism in the infertile couples. In this way the prevalence of the disease can be estimated in the selected group of women.

METHODOLOGY

It was a cross sectional study conducted in a private infertility clinic in the district of Punjab from January 2017- February 2020 (3 years). A total of 1516 subfertile patients were included. Temporal Sampling. All the subfertile patients fulfilling the inclusion criteria reported during study duration were enrolled for study. After taking informed consent from patients their blood samples and data were collected. After taking detail history of patients, confirming that at least more than one year of unprotected intercourse was practiced, failure to conceive a pregnancy they were enrolled in the study group. We Kept our screening tool to be TSH as the sole factor for detecting women with hypothyroidism. Blood samples were drawn and sent to the laboratory for assessment of TSH. All samples were analyzed in the same laboratory. Data was entered and ana-lyzed using SPSS -19. Mean and Standard deviation were calculated for quantitative variables like age. Frequency and percentages were calculated for qualitative variables like hypothyroid status.

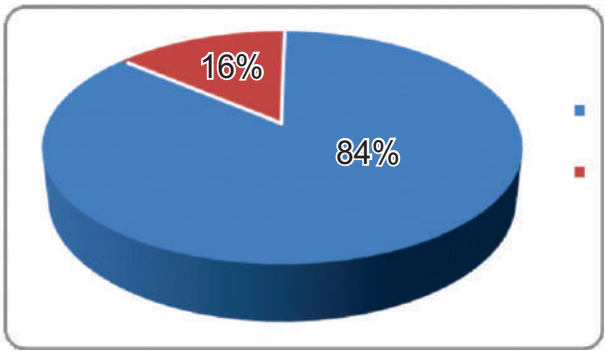
Inclusion Criteria: All women keen to conceive with primary and secondary infertility.

Exclusion Criteria: Women already taking thyroxin, and who were diagnosed cases of hypothyroidism.

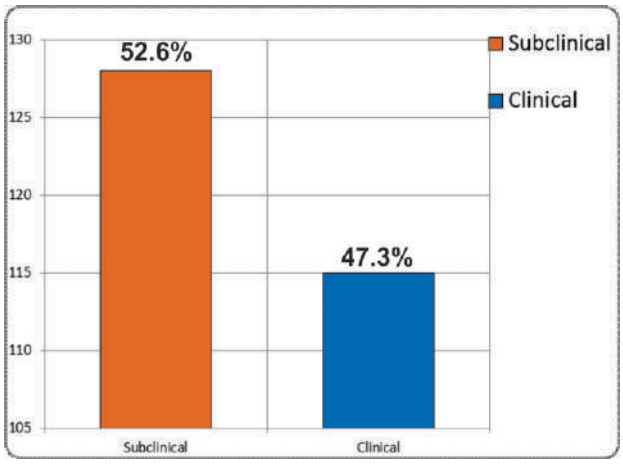
RESULTS

This study was conducted on 1516 patients of

reproductive age group age 18- 45 yrs. Who visited our infertility clinic from January 2017 to February 2020. After taking detail history and examination, there are blood was drawn for assessment of TSH. The data of 1516 patients were received and stored in our lab by the end of February 2020. It was observed that 243 patients had TSH above 4 iu. In this way 16% of infertile women were calculated to be hypothyroid. Amongst the 243 women of hypothyroidism 128 had mildly elevated TSH (4-6 iu) labeled as subclinical hypothyroidism, making a total percentage of 52.6% to be subclinical hypothyroid. Remaining 115 women were classified as clinical hypothyroidism, having TSH levels greater than 6iu, giving it a total percentage of 47.3%.



Graph 1: *Total Infertile Women Patients Screened - 1516. Number of Hypothyroid Patient Women - 243*



Graph 2: *Percentage of Subclinical Hypothyroid Women - 128 (52.6%). Percentage of Clinical Hypothyroid Women 115 (47.3%)*

DISCUSSION

In our geographical region, very fewer studies on hypothyroidism in infertility were seen. Studies worldwide have shown TSH plays a major role in the fertility of a patient. Preclinical studies suggest that thyroid hormone variation already within the normal range regulates the stimulatory effects of follicular stimulatory hormone and effect of growth of follicle and apoptosis suppression.[6] Murine and invitro studies suggest that thyrotrophe TSH and thyroid hormone are important factors during oocyte development and implantation.[16] Toherah Ojetal explained the role of TSH in un explained infertility. They showed in their 12 year study that women with unexplained infertility have higher TSH levels compare with the control population.[17] Another study by Tekehiro et al indicated a significant relationship between elevated TSH and decreased rate of clinical pregnancy. They also studied the relationship of TSH and unexplained infertility, and found that ovulatory disorders were significantly higher in patients with elevated[18] TSH and the incidence of unexplained infertility was higher in patients with elevated TSH. However they found in their study the frequency of elevated TSH to be 6.4% of the total infertile patients enrolled in their study. In our study we found that 16% of infertile women seeking for fertility treatment were hypothyroid with elevated TSH. Compared to this study our population is showing a greater frequency of the disease in the selected study population.

An Exclusive Study[19] done by priyanka sanjay et al on the different causes of infertility in their region have associated 21.6% of infertile population to be hypothyroid, the commonest among enodocrinological disorders in the infertile population enrolled in their study. Our observations coincide with their findings. They have emphasized greatly on the fact that hypothyroidism is surely prevalent in higher percentages in infertile women.

Study Conducted in a similar geographical region by Verma et al showed a much higher prevalence of 23.9% of hypothyroidism in infertile women. This study is quite similar to ours, showing greater preva-

lence of hypothyroid in infertile women. In our study amongst the 243 women, 128 were subclinical (52.6%), and 115 were clinical hypothyroid (47.3%). Verma et al in their study also assessed the percentage division of subclinical and clinical hypothyroidism. They found that 62.7% were subclinical and 37.3% were clinical hypothyroid. This approximates our results[7].

Preyatal at all studied the prevalence of hypothyroidism in infertile women and found that 53.7% of infertile women were hypothyroid. The sample of population they studied was very small; only 93 infertile women were studied for prevalence of hypothyroidism. But they were convinced by their study, that subclinical hypothyroidism was more common than clinical hypothyroidism. They reported 46.3 % women to be euthyroid, 50.5 % subclinical hypothyroid and 3.2% clinical hypothyroid.[5]

A Higher Percentage of women with infertility have shown frankly abnormal TSH levels as compared with controls in all studies observed.[20] Recent American Thyroid Association Thyroid and pregnancy guidelines recommend checking TSH in all women seeking evaluation for infertility. This is our recommendation too.[21] TSH a screening will not only increase the ability to conceive but also give favorable pregnancy outcomes.

CONCLUSION

Thyroid is a very important endocrine gland in the body, having profound effect on the fertility of a woman. Its disorder, primarily hypothyroidism has profound negative impact on a women's fertility. TSH is a simple, reliable, affordable, and readily available test in our country. All women with complaints of infertility should immediately be screened for hypothyroidism as prevalence of such a cause of infertility is found to be as high as 16%.

Limitations of Study

This is a prevalence study encompassing a large data set but limited number of exposure factors are probed because of confidentiality constraints.

Conflicts of Interest None

Funding Sources None

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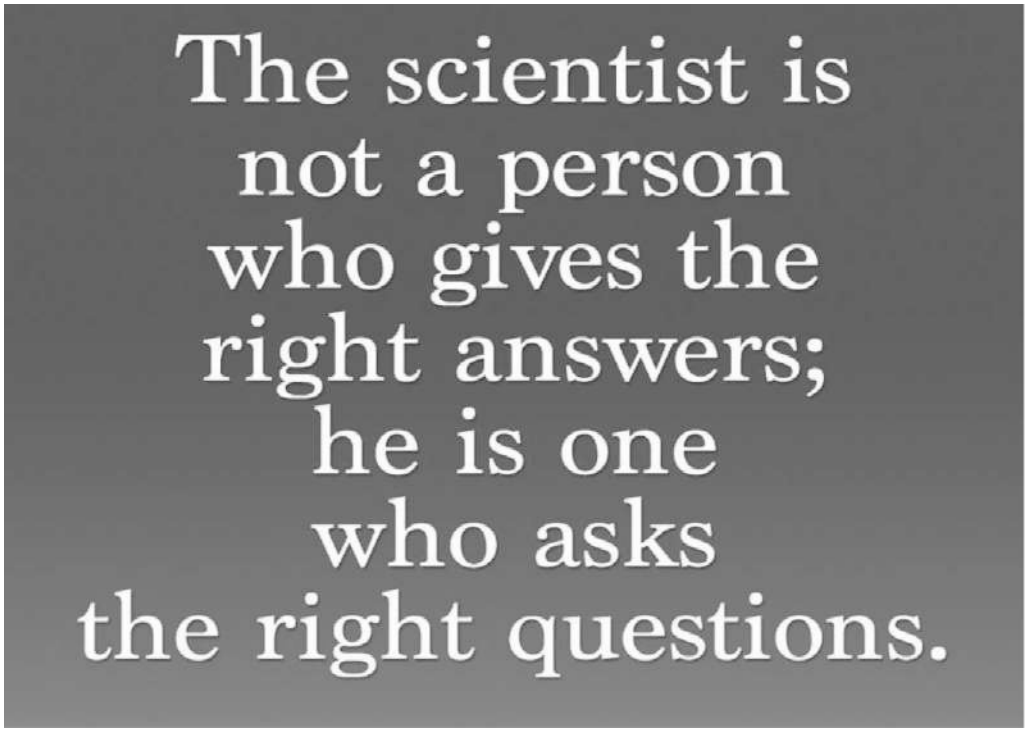

THE WIDESPREAD PRESENCE OF UTERINE LEIOMYOMAS: AN INQUIRY CONDUCTED IN MULTAN, PAKISTAN

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Abstract

Objective: To detect the prevalence of uterine leiomyomas in this area along with the analysis of its various types and association with parity and marital status. It was a descriptive observational study conducted at department of histopathology Bakhtawar Amin Medical & Dental Hospital, Multan from September 2020 to February 2021.

Methodology: All gynecological specimens received in histopathology laboratory were reviewed and counted. Out of one hundred and fifteen gynecological specimens received in the laboratory, fibroid cases were segregated and counted. Necessary data was recorded. Percentage and proportions were calculated for all the variables. Relevant tables and charts were computed.

Results: Out of one hundred and fifteen gynecological specimens, a total of 71 (61.7%) patients were found to have leiomyomas on histopathological examination. Most ladies presented in 3rd and 4th decades (mean age 41.45 years). Majority were married and multiparous. Menorrhagia was the commonest presenting complaint and intramural fibroids are the frequently noticed type.

Conclusion: Uterine leiomyoma is the frequently noticed benign gynecological pathology with striking association with married multiparous reproductive age ladies.

Key Words: Uterine leiomyomas, fibroids, histopathology

Leiomyoma also designated as fibroid is a benign smooth muscle neoplasm that can arise in any part of the body but most frequently arise in the uterus, where they usually present as menorrhagia (excessive menstrual bleeding) leading to anemia and may even cause infertility.[1,2]

In our histopathology laboratory we noticed presence of fibroids in almost every other gynecological specimen; this prompted us to study the frequency of fibroids in local population of this geographic region.

Uterine fibroids are slow growing, common, estrogen dependent, benign tumors. They are clinically evident in around 25-30% of women. However, their symptoms, number, size and location within the uterus vary from woman to woman.[3] They are usually discovered incidentally on abdominopelvic ultrasonography.[4]

According to various studies there is immense disproportion in the incidence and frequency of uterine myomas in various regions of the world.[3]

The principal approach of treatment is surgery; myomectomy for those ladies who want to retain their uterus and want to conceive and hysterectomy for those who have completed their families.[5,6]

Although they are benign in nature but at the same time they are the reason of significant distress

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in many women, so in order to improve the quality of life in women researches should be done to evaluate the actual burden of leiomyomas in every region with the aim that every area must devise an early detection plan accordingly to make women aware of the disease and to opt best treatment strategy.

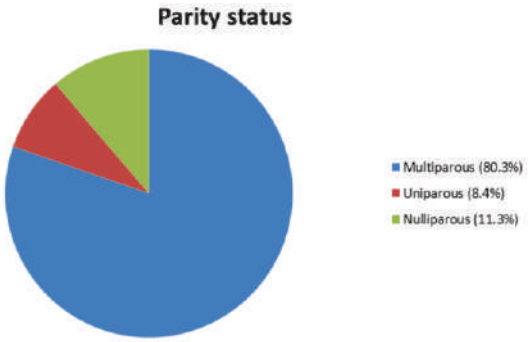
METHODOLOGY

This descriptive study was carried out at Bakhtawar Amin Hospital Histopathology Department over a period of six months from September 2020 to Feb 2021. Histopathology reports of all gynecological specimens were reviewed and counted. Out of 115 gynecological reports, fibroid cases were segregated and counted. Details like age, parity, presenting complaints, procedure opted and type and number of leiomyomata etc were recorded. Percentage and proportions were calculated for all the variables. Pertinent tables and charts were computed.

RESULTS

Out of 115 gynecological specimens, a total of 71 patients with fibroid uterus were segregated in histopathology department of Bakhtawar Amin Hospital, Multan. The mean age was 41.45 (ranging from 21-60 years). Most ladies presented in 3rd and 4th decade. Out of these 71 cases, two ladies were unmarried and sixty nine were married. Fifty seven (80.3%) were multiparous (mean parity 5), six (8.4%) were uniparous and eight (11.3%) were nulliparous. In majority, the cardinal trouble was menstrual disturbance mainly menorrhagia (53/74.6%); others presented as mass per vaginum (02/2.8%), pain/heaviness in abdomen (10/14.1%) and as a case of primary infertility in (06/8.5%). In 29 (40.8%) cases, multiple (max. thirteen) fibroids were found. The size range was between 0.5 cm to 17 cm in diameter. The most frequently noticed type was intramural.

In most of the cases (46/64.8%) myomectomy was done; in (2/2.8%) polypectomy; while in other (23/32.4%) cases, hysterectomy was opted.



Division of Cases According to Marital Status

Division of Cases According to Parity

DISCUSSION

Leiomyomas are the most frequent benign tumors of women in pelvis region[7,8] and forms a major bulk of gynecological disorders exerting influence on a large majority of women worldwide.[9,10]

Table 1: *Division of Cases according to Presenting Complaints*

Presenting complaint	Number of cases	Percentage %
Menstrual disturbances	53	74.6
Mass per vaginum	02	2.8
Abdominal pain/heaviness	10	14.1
Primary infertility	06	8.5

Table 2: *Number and Percentage of Various Types of Fibroids*

Type of fibroid	Number	Percentage %
Intramural	43	60.5
Submucosal	19	26.8
Submucosal leiomyomatous polyps	02	2.8
Subserosal	07	9.9

Several studies conducted in various regions of Pakistan reveal alarming occurrence of uterine fibroids especially in multiparous women.[11]

The frequency of uterine leiomyomas has been expanded worldwide and usually found out incidentally on clinical analysis and further investigations.[(12)]

The cause(s) for this widespread prevalence are yet ill defined. Several factors are considered among which genetic, hormonal, growth factors and racial factors grasp the most attention along with several other risk factors.[13]

The mean age in our study was 41.45 years almost in accordance with the studies conducted by Malik S N and Yu O et al where they found mean ages, 39.3, 44.8 and 40.4 respectively.[14,15]

Majority of these women presented in 3rd and 4th decades (32-48years) in keeping with the studies conducted by Kulkarni MR and Dayal S.[16,17]

Nearly all were married and a large majority was multiparous (80.3%) in accordance with several other studies.[18,4]

Menstrual abnormalities and pain abdomen were the common mode of presentation in our study comparable to the study by Geethamala K.[18]

In the present study, intramural fibroids were the most frequent. Many studies reveal that the intramural fibroid is the most common and widespread variety among all fibroids.[19,20]

Limitations

In this region of the world most ladies don't consult doctors especially for gynecological issues until and unless there is some marked health related disturbance; single unmarried ladies hardly reveal their gynecological problems as it is considered a social taboo and some sort of hindrance in marriage. This might be the reason we found mostly married and multiparous women in such studies. For exact evaluation of prevalence of fibroids large scale studies involving maximum number of ladies belonging to all ages should be conducted.

CONCLUSION

Leiomyomas are the commonest gynecological tumor noticed in this area; notably linked to marital status, parity, reproductive age and menstrual disturbances. Further researches on large scale are however, required to ascertain the exact prevalence of fibroids in this region.

Disclaimer

The abstract has not been previously presented or published in any conference, not a part of any research, PhD or thesis project.

Conflict of Interest None

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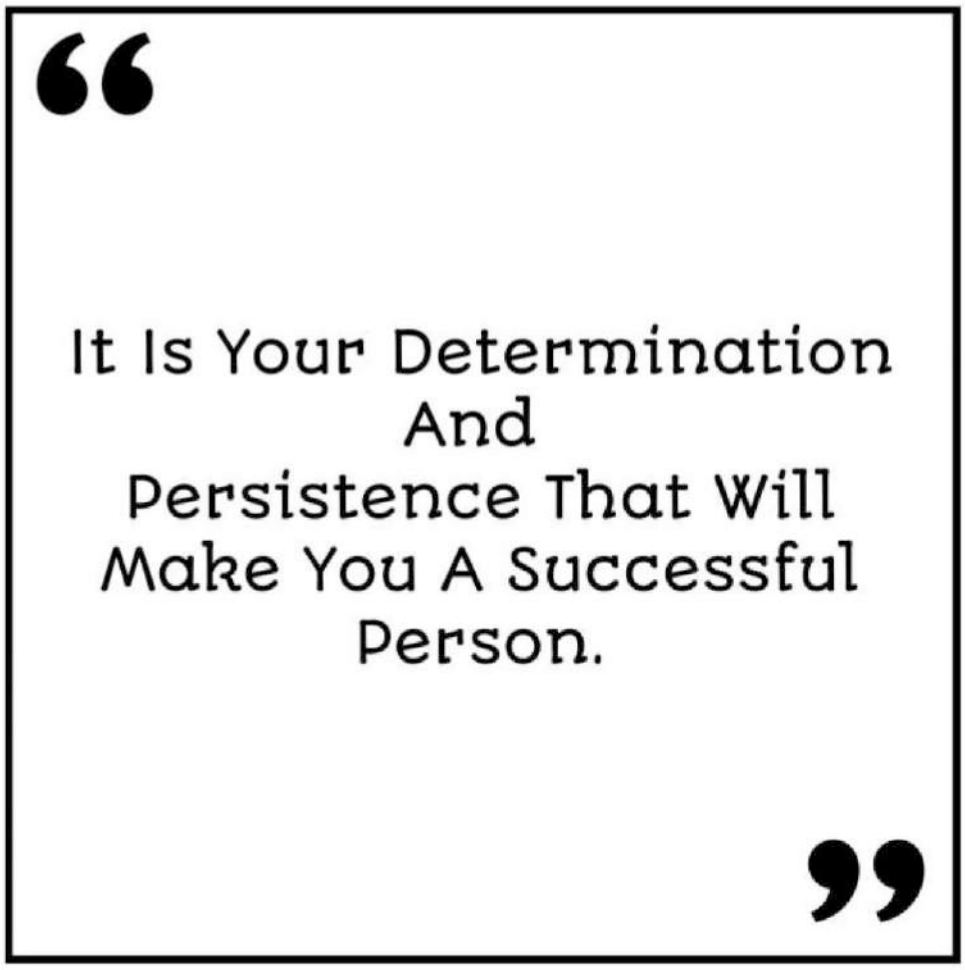

BREAST CANCER RISK ASSESSMENT IN PAKISTANI WOMEN USING GAIL MODEL

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Abstract

Objective: To find out five years and life time risk of developing breast cancer in Pakistani adult females using Gail model of risk assessment of breast cancer. This study will help in planning the prevention, early detection, treatment and thus reducing the mortality of the commonest malignancy of females.

Methodology: this is a cross-sectional study carried out among females presenting in out-patient department of Jinnah hospital/ Allama Iqbal medical college, Lahore from 1.7.2020 to 31.12.2020. The data was collected using convenience sampling method because of absence of sample frame and to ensure diversity of sample. The calculated sample size was two hundred. The data was collected according to a questionnaire designed from Gail model. The data was entered into SPSS version 21. The descriptive statistical analysis including mean, median, standard deviation, frequency distribution and percentage was used to calculate the numerical variables.

Results: This study was carried out on 200 adult females. The mean age of participants was 48.3 years(range 35-80 years) with standard deviation (SD) Of 11.46. Majority of the studied population was below 50 years of age and had menarche at the age of >13 years and first live birth between 20-24 years of age. Applying Gail model of risk assessment the mean 5 years breast cancer mean risk was .853, standard deviation (SD) was .4857. The minimum risk was 0.2% and maximum risk was 2.2% . Similarly the life time mean risk was 8.435% with standard deviation of 5.72 resulting minimum incidence of 1.1 and maximum 17.1%.The overall estimated life time risk was 14%.

Conclusion: Breast cancer is a major health issue in females. The 5 years and life time risk of breast cancer in Pakistani women is low as compared to other parts of world. Breast cancer risk assessment statistics can provide policy decisions regarding screening and early detection to health care providers.

Key Words: Breast cancer-risk assessment-Pakistani females.

Female breast cancer is the most prevalent cancer across the globe both in developed and developing countries.[1] Female breast cancer has now surpassed lung cancer as the leading cause of global cancer incidence in 2020, with an estimated 2.3 million new cases.[2] The risk of breast cancer is rapidly increasing in Pakistani females also. In Pakistan one in every nine women has a lifetime risk of being diagnosed with breast cancer.[3] The age standardized incidence rate of female breast cancer in Pakistan is one of the highest among Asian countries.[4] The well known risk factor of breast cancer are, being a female, family history of breast cancer, western race, young age of menarche and old age of menopause, hormonal replacement therapy, smoking, radiation, obesity in post menopausal women, denial of breast feeding, alcohol consumption and mutation in BARCA 1 and BARCA 2 genes. Majority of the above risk factors, are lacking in economically constrained countries like Pakistani population. Like other human cancers, efforts are being done to do the risk assessment for female breast cancers.

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Over the last two decades various statistical models have been designed to assess breast cancer risk as well, both at population and individual's level. Gail model is the most commonly and widely used model for breast cancer risk assessment.[5] It has been applied in different countries for its validity. Gail and his colleagues have also described another scoring model which includes body weight and mammographic density but excludes the age at onset of menarche.[6] In this study we tried to do 5 years and life long risk assessment of breast cancer in Pakistani female population using Gail model.

METHODOLOGY

This study was carried out at Jinnah hospital/ Allama Iqbal medical college, Lahore from 1.7.2020 to 31.12.2020, after the formal approval from the ethical review board of the institution. The study was cross sectional and was conducted among females presenting to various out patient departments for their health issues other than breast cancer. The data was collected using convenience sampling method because of the absence of sampling frame and to ensure diversity of sample. All participants were informed about the purpose of study and their verbal and written consent was obtained. It was also reassured that the collected data would be kept confidential and no breach in confidentiality would be accepted at any level of research. The data was collected using a questionnaire designed according to Gail model.[5] We calculated five years and life time risk of developing breast cancer among the sampled population. The variables of Gail model including ethnicity, age, age at menarche, age at first live birth, family history of breast cancer, previous history of breast biopsies or any atypia on breast biopsy were clearly asked and entered into the questionnaire. Data was entered in SPSS version 21. The descriptive statistical analysis including mean, median, standard deviation, frequency distribution and percentage was used to conclude the numerical variables.

RESULTS

This study was carried out on two hundred females. The mean age of the participants in this research was 48.3 years(range 35-80 years) with standard deviation (SD) of 11.46. The minimum age was 35.00 years and maximum age of the participant was 80.00 years. Majority of the studied population was below 50 years of age and had menarche at the age of >13 years and first live birth between 20-24

Table 1: Gail Model Risk Factors Frequencies Consolidated Table

Variables n= 200	Frequency	Percent
Age Mean=48.370, SD=11.46,Min=35.00, Max=80.00		
< 50 years	120	60.0
51 - 65 years	64	32.0
66 - 80 years	16	8.0
Age at menarche		
< 11 years	14	7.0
12 - 13 years	80	40.0
> 13 years	106	53.0
First Live Birth		
No Birth	14	7.0
< 20 years	40	20.0
20 - 24 years	72	36.0
25 - 29 years	54	27.0
> 30 years	20	10.0
1st degree relatives with Breast cancer		
No first degree relative with breast cancer	196	98.0
One relative with breast cancer	2	1.0
> 1 relative with breast cancer	2	1.0
Previous breast biopsy		
No biopsy	190	95.0
One biopsy	6	3.0
> 1 biopsy	4	2.0
Race/Ethnicity		
Asian	200	100.0
5 year breast cancer risk (%) Mean=.853 SD=.4857,Min=.2Max=2.2		
No risk (Gail score < 1.7)	190	95.0
Increased risk (Gail score > 1.7)	10	5.0
Lifetime breast cancer risk (%)Mean=8.435 SD 5.72, Min=1.1, Max=17.1		
No risk (Gail score < 1.7)	2	1.0
Increased risk (Gail score > 1.7)	198	99.0

years of age.(Table-1). Only 2% of females had first degree relative with breast cancer while only 5% of females had breast biopsy due to some reason and none of them had atypical hyperplasia of breast tissue. Applying Gail model, In five years the mean risk assessment was of 0.853% with standard deviation of 0.48%. The minimum risk being 0.2% and maximum 2.2%. (Table-1). Similarly the life time mean risk was 8.435% with standard deviation of 5.72% .The minimum risk being 1.1% and maximum 17.1%.

On further analysis of Gail model risk factors and age cross tabulation with Gail model risk score of more than 1.7 depicted 5years risk 0.0% up to 50 years and risk of 12.5% in females of 66-80 years of age (Table-2). Similarly in studied Pakistani women the estimated life time risk was 14%. (Table-2)

Table 2: *Gail Model Risk Factors and Age Cross Tabulation*

Breast cancer risk (%)	Age	Breast cancer risk (%)		Total	P value
		No risk (Gail score < 1.7)	Increased risk (Gail score > 1.7)		
5 year Breast cancer risk (%)	< 50 years	120	0	120	X^2=15.789, P< .000
		100.0%	0.0%	100.0%	
	51 - 65 years	56	8	64	
		87.5%	12.5%	100.0%	
	66 - 80 years	14	2	16	
		87.5%	12.5%	100.0%	
Lifetime breast cancer risk (%)	< 50 years	0	120	120	X^2=23.232. P< .000
		0.0%	100.0%	100.0%	
	51 - 65 years	0	64	64	
		0.0%	100.0%	100.0%	
	66 - 80 years	2	14	16	
		12.5%	87.5%	100.0%	

Five year and life time breast cancer risk was evaluated through Gail Model risk factors among three age strata.12.5% of subjects had increased 5 year breast cancer risk (%) (Gail score > 1.7) among 51- 65 years and 60-80 years strata of subjects, while No increase in 5-year breast cancer risk (%) was seen among age group < 50 years (p=.000). Lifetime breast cancer risk (Gail score > 1.7, 100.0% of subjects had increased risk(Gail score > 1.7) among less than 50 year of age and 51- 65 years and 87.5% of subject had increased life time risk among 66-80 years age (p=.000). (Table No:2)

Table 3: *Regression Model for 5 Year Risk of Gail Model with Risk Factors*

Model 5 year Breast cancer risk (%)	Unstandardized Coefficients		Sig.	95.0% Confidence Interval for B	
	B	Std. Error		Lower Bound	Upper Bound
(Constant)	.973	.212	.000	.556	1.390
Age	.006	.001	.000	.003	.008
Age of Menarche	-.089	.023	.000	-.135	-.043
First Live Birth	.037	.013	.007	.010	.063
First-degree relatives with breast cancer	.036	.086	.676	-.133	.205
Previous breast biopsy	-.060	.057	.294	-.174	.053

Table 4: *Regression Model for 10 year Risk of Gail Model with Risk Factors*

Model Lifetime breast cancer risk (%)		Unstandardized Coefficients		Sig.	95.0% Confidence Interval for B	
		B	Std. Error		Lower Bound	Upper Bound
1	(Constant)	2.094	.105	.000	1.887	2.301
	Age	-.002	.001	.000	-.004	-.001
	Age of Menarche	.006	.012	.634	-.017	.028
	First Live Birth	-.001	.007	.885	-.014	.012
	First-degree relatives with breast cancer	-.011	.042	.792	-.095	.073
	Previous breast biopsy	.009	.028	.744	-.047	.065

Table No. 3 and 4 depicts about the relationship between the independent variables and the dependent variable (Lifetime breast cancer risk (%)). These estimates tell the value of increase in Gail scores that would be predicted by a 1 unit increase in the predictor. /(independent variables like age, age of menarche, live birth, first-degree relatives with breast cancer and previous breast biopsy).

Regression model for 5 year risk using Gail Model was predicted for risk factors like age, age of menarche, live birth, first-degree relatives with breast cancer and previous breast biopsy. This explains how much risk for cancer increases with change in these independent variables. So, for every unit increase in age, a .006 unit increase in Gail score is predicted,

holding all other variables constant or we can say, for every increase of one point age, Gail score is predicted to be higher by .006 points, and this increase is statistically significant. (p= .000).

For every unit increase in age at menarche, there is a-.089 unit decrease in the predicted Gail score, holding all other variables constant and this increase is statistically significant. (p= .000).

Similarly a 037 increase in Gail score is predicted, with first live birth that was also statistically significant (p=.007) and .036 unit increase can be predicted for Gail score for first degree relative with breast cancer but relationship was not significant (p= .676), and similarly a decrease in Gail score by -0.060 can be predicted for previousbreast biopsy which is also non-significant. (p=.294). (Table no: 3).

Regression model for life time risk using Gail Model was predicted for risk factors like age, age of menarche, live birth, first-degree relatives with breast cancer and previous breast biopsy. That how much risk for cancer increase with change in these independent variables. So, for every unit increase in age, a -0.002 unit decrease in Gail score is predicted, i.e Gail score is predicted to be lower by -0.002 points, and this decrease is statistically significant. (p= .000).

For every unit increase in age at menarche, there is a .006 unit increase in the predicted Gail score, holding all other variables constant and this increase is statistically non-significant. (p= .634). A -.001 decrease in Gail score is predicted, with first live birth that was non-significant (p= .634) and a -.011 unit decrease can be predicted for Gail score for first degree relative with breast cancer but relationship was not significant (p= .792), and similarly a increase in Gail score by .009 can be predicted for previous breast biopsy which is also non-significant. (p=.744). (Table no: 4).

DISCUSSION

Breast cancer is the most common female cancer around the world.[7] The most frequently diagnosed and leading cause of cancer death, however, the incidence varies across the countries.[8] Due to this fact there is lot of anxiety and breast cancer phobia in general and especially when familial predisposition is considered. Dr. Mitchell Gail and his co-workers devised a statistical algorithm in 1989 after screening of 280,000 females 35 to 74 years of age. Originally this model was tool of risk assessment in white women but later on other studies on African-American and Hispanic population also resulted in accurate risk assessment. Gail model does risk assessment on the following risk factors;[9]

1- Age
2- Body mass index
3- Age at menarche
4- Obstetric history
5- Age at menopause(if applicable)
6- History of benign breast disease that increases the breast cancer risk like LCSI, hyperplasia, atypical hyperplasia
7- History of ovarian cancer
9- Use of hormone replacement therapy
10- Family history

The risk assessment helps in making strategies for screening. High risk women will be included in surveillance and screening and at the same time low risk women may be excluded thus reducing the burden of expenses in health care model. There are various risk assessment tools and models for breast cancer but the most extensively used model is Gail model.[10] the other models and tools to estimate risk of breast cancer are Claus model[9], Cuzick-Tyrer model and BRCAPro. There are pros and cons in each risk assessment protocol. BRCAPro estimation variable mainly involves BRCA 1 and BRCA 2 mutation frequencies thus is applicable only on the hereditary breast cancer.[10] The other considerations are ethnicity and age of salpingo-oophorectomy. Similarly Claus model is applicable in females having family history of breast cancer. Unlike Gail model, Claus model includes the number and ages of onset of breast cancer in first and second degree relatives. The Gail model was designed at the National Institute and the National Surgical Adjuvant Breast and Bowel Project. The main limita-

tion of Gail model is that it surveys only first degree relatives which under estimates the breast cancer risk, moreover, Gail model does not consider the age of onset of breast cancer.[11]

In this study we found the 5yrs breast cancer risk of maximum 2.2% with mean of 0.85% and SD of 0.4857% which is quite less than similar other studies as depicted in Table No 3. In Turkish women it is 0.88% ± 0.91% (0.2 ± 8%). In Turkish population the 5 years risk is 0.8% and lifetime risk is 9.37%

Table 5: Comparison of the Result of Our Study with the Studies of other Authors

Study	Country	Sample size	Age	Five-years risk	Lifetime risk
Rubab A et al, 2021	Pakistan	200	>35	0.85	8.4
Al Otaibi HH 2017 (13)	Saudia Arabia	180	>35	0.87	9.6
Bener et al, 2017 (14)	Qatar	1488	>35	1.12	10.57
Ewaid and Al-Azzawi, 2017 (15)	Iraq	250	>35	0.95	11.3
Khaliq et al, 2016 (16)	USA	250	>50	1.67	-
Mirghafourvand et al, 2016(17)	Iran	560	>35	0.6	8.9
Khazaee-Pool et al, 2016 (18)	Iran	3847	>35	1.61	11.71
Erbil et al, 2015 (12)	Turkey	231	>35	0.88	9.37
Eadie et al, 2013 (19)	UK	355	>46	1.5	9
Fikree and Hamadeh, 2013(2O)	Bahrain	300	>35	0.7	9.3

similarly in USA the 5 yr risk is 1.67% 12

In British women the 5yr risk is 1.5% whereas lifetime risk is 9%. The results of similar studies of Gail model in other regions are comparable to this study. (Table N0:5) Fast tract westernization of Pakistani society is leading to a rapid increase in incidence of female breast cancer. This fact has been validated by both cross sectional data[21] as well as prediction statistical models.[22] The main purpose of risk assessment is do screening for these selected females. Breast cancer screening guidelines increasingly recommend that clinician perform shared decision making for screening.[23]

In this study the findings of individual risk factor like age, age at menarche, age at menopause, family history, history of benign breast disease and history of ovarian tumor are similar to other publications. The main limitation of this research is due to it cross sectional design which does not allow to record any change over a period of time. Moreover, convenience sample was used from only one place which may not be the representative of entire population.

CONCLUSION

Breast cancer is a common health issue of women in Pakistan. This disease needs some methodology of risk assessment so that guidelines of screening can be developed. Gail model is an easily applicable statistical tool for breast cancer risk assessment. Regarding the lack of screening strategies of breast cancer in Pakistan, it seems that screening must be stressed in women with a high risk of breast cancer.

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Conflict of Interest

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SEVERITY AND PATTERNS OF HAIR LOSS IN PATIENTS INFECTED WITH COVID-19 INFECTION

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Abstract

Background: COVID -19 pandemic has a unique global impact .The objective of this study was to evaluate the severity of hair loss and its psychological impact in patients affected with COVID -19 infection .

Methodology: In this case series a total of 180 patients affected with COVID -19 infection were enrolled after informed consent. Patients were evaluated for the presence excessive hair fall during or after the COVID -19 illness with the help of detailed history and examination. All information was recorded on predesigned proforma.

Results: A total of 180 patients ,mean 46.5 age years were studied. Excessive hair fall was reported in 119 patients (66%) while no excessive hair fall was appreciated in 61 patients (34%).Mental stress due to hair fall was found in 108 patients (60%) while no stress was seen in 72 patients (40%).Severity of hair fall was mild in 38 patients (21%),moderate in 52 patients (29%) and severe in 90 patients (50%).

Conclusion: Our study suggests that significant number of patients affected with COVID -19 infection have reported hair loss with a marked psychological impact .

Key Word: hair loss, COVID -19 infection, pandemic , psychological impact

COVID-19 illness is a highly contagious respiratory tract disease caused by Coronavirus 2 (SARS Cov2), which was first reported on December 1, 2019 from Wuhan, China.1 COVID-19 outbreak has been declared a pandemic by the World Health Organization on March 11, 2020 and as of April 26, 2020, approximately 3 million cases were identified worldwide and more than 200 thousand deaths occurred. SARSCoV2 is transmitted through virus containing droplets and contaminated objects.[1,2]

The patients suffering from Coronavirus infection have developed various cutaneous manifestations during their illness including urticaria, vasculitis, purpura ,livedo reticularis and pseudochillblains[2]. In addition to these manifestations many of the patients suffering from corona virus infection have reported hair loss of varying severity and patterns. There are different causes of hair loss in these patients including tellogen effuvium, alopecia arreata , and seborrhic dermatitis and aggravation of the pre existing androgenetic alopecia in males and female pattern baldness in women.[3]

The hair cycle consists of three stages: anagen, catagen, and telogen. The anagen phase is the growth phase of the hair cycle. Approximately 85% of hairs are in the anagen phase at a time and this phase lasts between 2 and 6 years. The catagen phase is the transition phase, which occurs when anagenic follicle receives a signal and it ends the growth phase. The catagen phase lasts for 1 to 2 weeks. The telogen phase, which is also known as the resting phase, is the last stage of the hair cycle. This phase lasts 5 to 3 weeks until the anagen phase is restarted.[3,4] Telogen effluvium

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is a very common form of hair loss that is characterized by a diffuse hair loss resulting from the hair's entering the telogen phase early. Inducing factors can be listed as systemic diseases, stressful events, drugs, nutritional deficiencies, and major surgery. It occurs 3 months after the event that causes hair loss and it generally restricts itself, it lasts for about 6 months (acute TE). There is also a chronic form of TE in which the period of hair loss exceeds 6 months.[3]

Patients with Tellogen effuvium usually women, are often deeply anxious, reporting not sleeping or waking up in the night with their hair as their first thought. Tellogen effuvium may have a profound impact on the patient's psychological health causing disturbance of sleep, eating habits and loss of concentration at work place.[4]

The data obtained in the study carried out by Turkmen D et al. showed that there were a large number of especially Tellogen Effuvium patients during the short pandemic process and that a great majority of these patients did not receive treatment to avoid the risk of COVID-19.[3] Considering that Tellogen Effuvium increases 3 months after stressful situations, we can anticipate that the number of patients will increase gradually in the future.

The patients having hair loss during this illness can be evaluated and managed accordingly to avoid the stress related to hair loss in these patients.

METHODOLOGY

This study was carried out in Dermatology unit 1 , Jinnah hospital, Lahore from November 2020 to April 2021.Patient information and identity were kept confidential. The study population included both health care professionals and general public.

A total of 180 patients were enrolled. After informed consent basic information regarding age, gender, duration of COVID -19 illness, history of excessive hair fall, pattern of hair fall and psychological impact of hair fall were obtained. Patients were also examined under good light to see for the patterns of hair loss and also subjected to hair pull test.

Approval was obtained from Ethical Review Board Allama Iqbal Medical College /Jinnah hospital, Lahore in its 77th meeting on 24/11/2020.Written informed consent were obtained from all patients included in the study.

RESULTS

In this study there was a total of 180 patients. The mean age of the patients was 46.5 years, with the maximum age of 71 years and the minimum age of 23 years. There were 104 males patients (58%) and 76 female patients (42%) in this study. Excessive hair fall was reported in 119 patients (66%) while no excessive hair fall was reported in 61 patients (34%). Duration between start of COVID -19 symptoms and the start of hair loss was less than 1 month in 14 patients (8% of patients), less than three months in 49 patients (27% of patients)and was more than 3 months in 117 patients (65% of patients) respectively. Distribution of hair loss was generalized in 119 patients (66% of patients), however it was localized in 61 patients (34 % of patients). Severity of hair loss according to number of hair loss per day was less than 50 hair in 18 patients (10 % of patients),more than 50 in 72 patients (40 % of patients)and more than 100 in 90 patients (50 % of patients. Hair pull test was found to be positive in 54 patients (30 % of patients) and was negative in 126 patients (70 % of patients). Severity of symptoms of COVID-19 infection were mild in 38 patients (21 % of patients), moderate in 52 patients (29 %)of patients and severe in 92 patients (51 % of patients).There was no previous history of anxiety or depression in 135 patients (75% of patients),however there was positive history of depression and anxiety in 45 patients (25 % of patients). Hospital anxiety and depression scale was used as a tool to assess psychological impact of hair loss associated with COVID -19 infection. The score was normal in 72 patients (40 %of patients), borderline In 90 patients (50 % of patients) and was severe in only 18 patients (10% of patients). Disturbance of sleep was experienced by 70 patients (39 % of patients) however there was no sleep disturbance in 110 patients (61% of patients). Disturbance of appetite was reported

by 41 patients (23% of patients), however no disturbance of appetite was reported in 139 patients (77% of patients). Disturbance of concentration of work was reported by 36 patients (20% of patients), however in 144 patients (80 % of patients) there was no affect on concentration at work. Stress due to hair loss after COVID -19 infection causing disturbance of sleep, appetite and loss of concentration at work was mild in 97 patients (54% of patients), moderate in 47 patients (26% patients), and was severe in 36 patients (20% of patients)respectively. Thus there was significant hair loss in patients affected with COVID -19 infection (p value<0.05).

Table 1: Hair Loss Profile

Parameter	Frequency	Percentage
Excessive Hair Fall		
Yes	n=119	66%
No	n=61	34%
Duration Of Covid		
<1 month	n=14	8%
>3 months	n=49	27%
>6 months	n =117	65%
Distribution Of Hair Loss		
Generalized	n=119	66%
Localized	n=61	34%
Severity Of Hair Loss		
<50	n=18	10%
>50	n=72	40%
>100	n=90	50%
Severity Of Covid Symptoms		
Mild	n=38	21%
Moderate	n=52	29%
Severe	n=90	51%

Table 2: Psychological Assessment Profile

Parameter	Frequency	Percentage
Previous History Of Anxiety And Depression		
Yes	n=135	75%
No	n=45	25%
Hospital Anxiety And Depression Scale		
Normal	n=72	40%
Borderline	n=90	50%
Severe	n=18	10%
Disturbance of sleep		
Yes	n=70	39%
No	n=110	61%
Disturbance of appetite		
Yes	n=41	23%
No	n=139	77%
Loss of concentration at work		
Yes	n=36	20%
No	n=144	80%

DISCUSSION

In our study we evaluated a total of 180 confirmed cases of COVID -19 infection with a mean age of 46 years. The results showed that people of all ages were affected with the majority of middle aged people. There were more males as compared to females in our study. This could be due to the fact that males were more frequently affected in the first wave of infection and secondly there was a greater ratio of males presenting to the hospital as compared to the females.

This study also revealed that most of the cases experience hair loss after a period of three months suggesting that in most of the patients it became a chronic phenomenon.

In our study population generalized hair loss was appreciated in most of the cases especially the females, however in some localized pattern was seen especially the temporal areas. In a study carried out by Andy Goren et in Spain a male pattern of hair loss was reported among hospitalized COVID-19 patients which gives a clue that androgen expression in these patients may be related to the severity of COVID infection.

When assessing for severity of hair loss a directly proportional relation was appreciated between the severity of COVID-19 infection and the hair loss. Most of the patients in our study were those who suffered moderate to severe illness. This could probably be explained by the fact that most of the patients suffering from mild to moderate illness were managed at home. Secondly there were periods when the Dermatology outpatient departments were closed to minimize the spread of COVID-19 infection thus contributing towards less presentation of patients in the out patient department will mild to moderate hair loss.

In our study we have also evaluated the psycho-

logical impact of hair loss in patients who suffered from COVID-19 infection. Patients suffered stress during this pandemic which was multifactorial. Stress due to the disease itself, stress due to the quarantine, loss of jobs ,financial insecurity due to lock downs and uncertain circumstances all over the globe. We tried to evaluate the stress due to hair loss using the Hospital anxiety and depression scale which reflected impact of stress due to hair loss in these patients was significant.

In our opinion hair loss is a common response to any element of physical or mental stress. Similar is the case with COVID -19 infection which has caused significant physical and mental stress thus aggravating hair loss in these patients as reported by a Chinese study published in The Lancet which showed that 22 % of hospitalized COVID-19 patients in China reported hair loss six months later.

Another observation is that many people are now aware of COVID-19 and its symptoms and the previously unnoticed hair fall after any illness is now very easily related with the COVID -19 infection.

CONCLUSION

This study emphasizes the importance of early diagnosis of previously existing factors contributing to hair loss and introduction of supportive therapies to minimize hair loss and thus subsequent stress in patients suffering from hair loss post COVID -19 illness.

Author's Contribution

SR,ZN: Concept, data collection, analysis, write up.

KTM: Data collection, analysis

LMM,TR:Concept , analysis, write up

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FREQUENCY OF FATIGUE AMONG PATIENTS WITH LOCALLY ADVANCED BREAST CANCER

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Abstract

Background: Fatigue is a common symptom experienced by cancer patients which a part from clinical manifestation of disease, is common side effect of cancer treatment like chemotherapy and radiotherapy. This study investigates the frequency of fatigue and identifies the demographic, clinical, and lifestyle factors associated with cancer-related fatigue (CRF) in breast cancer patients undergoing chemotherapy.

Methodology: It is a cross sectional study, conducted at Department of Oncology, King Edward Medical University, Lahore. All patients of locally advanced Breast cancer (stage 2, 3) were included in the study after taking informed consent. Standard Fatigue scale was used to assess provenance of Fatigue. Collected data was entered and analyzed using statistical package for social sciences (SPSS) version 23. An initial frequency counts and percentages were obtained for all the data. Descriptive statistics were reported as means, frequencies and percentages. Intergroup comparisons were performed using Chi--Square test. All p values<0.05 were reported as statistically significant.

Results: Total 100 patients were included with mean age 47.1±12.4 years. Fatigue was found to be present in 87% patients. On stratification of data, fatigue was seen more in patients with BMI >25 kg/m² (90%) than in those with BMI <25kg/m² (84%).

Conclusion: Fatigue is very common among Breast cancer patients. Larger studies are required to address its burden and formulate effective management strategies to manage cancer related fatigue (CRF).

Key Words: Cancer related fatigue, advanced Breast Cancer, Standard Fatigue scale.

Fatigue is recognized as one of the most common adverse effects of cancer that might persist for years after completion of treatment in otherwise healthy survivors. Cancer-related fatigue is defined as a distressing, persistent, subjective sense of physical, emotional, and cognitive tiredness or exhaustive related to cancer or cancer treatment that is not proportional to recent activity and interferes with usual functions.[1]

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For cancer patients, fatigue includes decreased physical performances, extreme unusual tiredness, weakness, which is distinctly different from healthy person. Cognitive distress is particularly prominent.[2,3] The major determinants of long-term fatigue are pre-existing psychological or depressive disorders, migraine, analgesic use, peripheral arterial obstructive disease, arthritis plus inactive lifestyle. Radiotherapy and chemotherapy imparts its contribution during treatment phase. Insomnia occurs in 30% to 50% of cancer population, with pain as a major contributor to insomnia ultimately leading to fatigue.[4]

Studies have shown that in various cancers, alterations occur in inflammatory cytokine genes, leading to altered inflammatory process which in turn contributes to cancer related fatigue.[5-12] It is hypothesized that fatigue associated with adjuvant radiation is related to tissue damage. Cancer related

fatigue found to be more common with chemotherapy than radiotherapy among breast cancer patient.[13] Cancer is a major health problem in developing countries like Pakistan.[14] Currently there are no proper guidelines for fatigue assessment and management. The rationale of our study is to highlight the frequency of fatigue and various factors associated with it in a resource poor country like Pakistan.

METHODOLOGY

It is a cross sectional study, conducted at Department of Oncology, King Edward Medical University, Lahore. All patients of locally advanced Breast cancer (stage 2, 3) were included in the study after taking informed consent. Standard Fatigue scale was used to assess prevalence of Fatigue. Collected data was entered and analyzed using statistical package for social sciences (SPSS) version 23. An initial frequency counts and percentages were obtained for all the data. Descriptive statistics were reported as means, frequencies and percentages. Intergroup comparisons were performed using Chi--Square test. All p values<0.05 were reported as statistically significant.

RESULTS

Total 100 patients were included with mean age 47.1±12.4 years. Fatigue was found to be present in 87% patients. On stratification of data, fatigue was seen more in patients with BMI >25 kg/m² (90%) than in those with BMI <25kg/m² (84%).

DISCUSSION

Table 1: Demographics of Patients Involved in Study

Demographics	Frequency (n)	Percentage (%age)
Age (years)	47±12.4	
BMI (kg/m²)	24.0±6.5	
ECOG performance status	1.7±0.9	
Stage of disease		
Stage 2	87	87
Stage 3	13	13
Duration of symptoms		
<6months	26	26
>6 months	74	74

Table 2: Percentage of Fatigue Among Various Subgroups

Parameter	Percentage (%age)
BMI (kg/m²)	
<25kg/m²	84.4
>25kg/m²	90.47
ECOG	
0-2	86.84
>2	87.5
Stage of disease	
Stage 2	87.35
Stage 3	84.61

Cancer survivors comprise a vulnerable population who experience disease and treatment-related physical and mental symptoms. Fatigue is one of the most frequently reported symptom,[15,16] which affects 60-96% of cancer patients, including 60-93% of those receiving radiotherapy and 80-96% being treated with chemotherapy.[17,18]

Cancer-related fatigue (CRF) is far more distressing than fatigue experienced by other individuals and is less likely to be relieved by rest. Patterns of the occurrence of fatigue may differ according to the type of treatment.[19] Breast cancer is notable for causing long-term treatment effects that begin during the treatment period and continue after therapy.[20] Certain symptoms are more prominent in women with breast cancer, including fatigue, hot flashes, sexual dysfunction, infertility, bone loss, and cognitive dysfunction.[21] Studies indicate that the prevalence of fatigue is high in patients with breast cancer; as many as 99% of these patients experience fatigue during the course of treatment. CRF could be attributed to endocrine disrurbances as a result of breast cancer treatment, including induction of amenorrhea, the induction of premature menopause due to ovarian toxicity caused by chemotherapy, radiotherapy and the side effects of adjuvant endocrine treatment.[22] Hormonal changes due to endocrine therapy, cytokine release, increased tumor growth, impaired energy transformation processes and other pathological changes due to disease contribute to CRF.[23,24] It imposes detrimental effects on functional quality of life of cancer patients.[25]

The phenomenon of CRF is complex and multi-

factorial and is currently not fully understood.

A study by Banipal et al, demonstrated fatigue in 83.1% cancer patients with intensity of fatigue stays stable throughout the treatment cycles.[26] A reason for the stability could be habituation to the experience of fatigue. In our study, we found CRF to be present in 87% of patients which is very similar to previous data. These results make cancer related fatigue a major problem in these poor souls who are fighting with cancer which adds to their misery. There are many limitations in this study which include small sample size, stratification with respect to various chemotherapy regimens.

CONCLUSION

Fatigue is very common among Breast cancer patients which leads to impairment of their quality of life. Larger studies are required to address its burden and formulate effective management strategies to manage cancer related fatigue (CRF).

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FREQUENCY OF HYPOMAGNESEMIA AMONG PATIENTS OF ACUTE RENAL FAILURE PRESENTED IN TERTIARY CARE HOSPITAL

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Abstract

Background: Acute kidney injury is associated with many electrolyte disturbances like hyperkalemia, hyperphosphatemia, hypocalcemia, hypomagnesemia and bicarbonate deficiency. Hypomagnesemia is associated with non-recovery of AKI and is clinically manifested as neuromuscular, neuropsychiatric and cardiotoxic manifestations. Data available regarding frequency of hypomagnesaemia among patients of acute renal failure is scarce so current study was undertaken.

Objective: The objective of this study was to determine the frequency of hypomagnesemia among patients of acute renal failure presenting to the tertiary care hospital.

Methodology: This cross-sectional study was conducted at Jinnah hospital Lahore from 1st August 2020 to 31st January 2021. About 130 patients with acute renal failure fulfilling the inclusion criteria were included in the study. Non probability consecutive sampling was used to enroll the patients in the study.

Acute kidney injury was defined as having either increase in serum creatinine by > 0.3 mg/dl from baseline within 48 hours of admission or increase in serum creatinine to > 1.5 time's baseline within prior 7 days or urine volume < 0.5 ml/kg/h for 6 hours. Hypomagnesemia was labeled as serum magnesium levels of < 1.7 mg/dl.

Results: Patients ranged from 23 to 70 years in age. The mean age of the study population was 45.9 ± 12.9 years. Of them 67 patients (51.5%) were male and 63 patients (48.5) were female. The biochemical finding of hypomagnesemia was noted in 56.7% of the patients (n= 75). The tendency towards hypomagnesemia was noted in elderly population having elevated baseline serum creatinine. No significant gender variation was observed in our study.

Conclusion: It was noted that frequency of hypomagnesemia among patients of acute renal failure was high. A screening measure need to be considered for hypomagnesemia.

Key Words: Hypomagnesemia, acute renal failure, magnesium, kidney disease, electrolyte imbalance.

Acute kidney injury also termed as acute renal failure is a frequently encountered medical condition in acute medical units worldwide. Around 13.3 million patients per year suffers acute renal failure and about 1.7 million deaths per year reported due to acute renal failure.[1] Acute renal failure includes a variety of clinical patterns ranging from mild to severe renal injury that may result in complete renal shutdown.[2] Many different classification criteria are used clinically to define AKI. RIFLE and AKIN are the most eminent of them, which also have correlation with morbidity and mortality associated with the AKI.[3] The estimated prevalence of acute renal failure ranges from 1% to 70% based on different criteria.[4,5] The different mechanisms of AKI include failure of

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kidney to get rid of nitrogenous waste, manage electrolytes, regulating the intravascular volume and the acid-base balance.[6] The AKI has many devastating clinical impacts that invariably increase mortality and morbidity[7]. AKI can lead to chronic kidney disease and follow up after one year of AKI has shown substantially high risk of developing CKD.[8]

Electrolyte imbalance is a potentially life-threatening complication associated with AKI, which needs prompt identification and management. These include potassium, calcium and phosphate imbalances in general. However, magnesium levels are not routinely checked in this context. Hypomagnesemia can have detrimental effects in AKI mainly by further reducing the blood flow to the kidney and worsening the ischemic insult to the kidney.[9] However, studies regarding the effect of renal failure on magnesium in body are scarce. Only a few studies are available so far in which the patients of acute renal failure have very high percentage of hypomagnesemia. In one of those studies frequency of low magnesium was significantly high i.e. 62%.[10] As a dearth of literature exists regarding frequency of hypomagnesemia in patients of acute renal failure on international as well as local level. Furthermore, hypomagnesemia is clinically manifested as neuromuscular and neuropsychiatric symptoms which are clinically masked by hyponatremia, and hypomagnesemia is often overlooked by clinicians. Hypomagnesemia is associated with long term depression, cardiotoxicity and neurological manifestations including vertigo, tremor, nystagmus, ataxia, hyperreflexia and fasciculations.[11,12] Hypomagnesemia is also associated with increased risk of arterial hypertension, dyslipidemias, insulin resistance, diabetes, coronary artery disease and arrhythmias.[13]

The rationale of our study was to find out the frequency of hypomagnesemia in patients of acute renal failure presenting to tertiary care hospital. This can help identify magnesium deficiency earlier in the course of AKI, thus preventing further decline in GFR solely due to it.[13] Thus, this study will provide information regarding the frequency of hypomagnesemia in patients of acute renal failure. This will give an idea to the clinicians regarding the magnitude of problem in these patients and for early diagnosis and management to avoid morbidity associated with this condition. The objective of the study was to determine the frequency of hypomagnesemia among patients of acute renal failure presenting to the tertiary care hospital.

METHODOLOGY

This cross-sectional study was conducted at Jinnah hospital Lahore from 1st August 2020 to 31st January 2021. After informed consent, by using non-probability consecutive sampling,130 cases were enrolled during the 6-month study period who were presented with acute kidney injury and fulfilling the inclusion criteria. Acute renal failure was defined as having any one of the following, rise of serum creatinine by > 0.3 mg/dl from baseline within 48 hours of admission or rise of serum creatinine to > 1.5 times baseline, which is presumed to have occurred within the prior 7 days or decrease in volume of urine to < 0.5 ml/kg/h for 6 hours.

Hypomagnesemia was defined as having serum magnesium levels < 1.7 mg/dl.

Inclusion criteria

Patients of age 15 to 70 years.

Male and female genders.

Patients having acute renal failure (as per operational definition) presented to tertiary care hospital were included in the study.

Exclusion criteria

Patients not willing to participate in the study. Patients with MOF, on ventilatory support, having drug-induced acute renal failure, obstructive kidney disease, diabetics, alcohol addicts or having serum albumin levels < 3 mg/dl were excluded from the study.

About 130 patients of AKI presenting to the Jinnah hospital Lahore who have matched with our inclusion criteria were approached. Before enrolling in the study an informed consent was taken from them. Information regarding their demographic data was noted in the performa. Blood samples were taken by following aseptic measures and were sent immediately

to the pathology laboratory of same institute in the standard serum viols. The results of serum magnesium were collected next day by the researcher and were noted in the performa for the presence of hypomagnesemia. Confidentiality of the data was ensured. Patients were managed according to hospital protocols.

Analysis of data was done with SPSS version 21.0. Numerical variable i.e. age was summarized as mean and standard deviation. Qualitative variables like sex and presence of hypomagnesemia were presented in the form of frequency and percentages. Data was stratified for age and gender and baseline serum creatinine. Chi square test was applied to check statistical significance post-stratification. P-value <0.05 was taken as significant.

RESULTS

130 patients were included in our study population ranged from 23 to 70 years in age. The mean age of the study population was 45.9 ± 12.9 years. In our study population (n=130), 62 patients (47.7%) were below 45 years and 68 patients (52.3%) were either 45 years of age or above. Of them 67 patients (51.5%) were male and 63 patients (48.5) were female. The biochemical finding of hypomagnesemia was noted in 56.7% of the patients (n= 75).

When study population was distributed along with baseline serum creatinine, mean value came up 8.97 ± 2.61mg/dl ranged from 4.5 to 13 mg/dl. When study sample was distributed along creatinine group, 85 patients (65.4%) had creatinine below 10mg/dl and remaining 45 (34.6%) had above 10mg/dl.

When we cross tabulated age group with hypomagnesemia and used pearson chi square test, it showed significant results (p=0.016) that describes an unequal distribution between both age groups regarding hypomagnesemia. (Table I) On cross tabulating hypomagnesemia with gender, results came up statistically insignificant that showed unequal distribution of hypomagnesemia among male and females. (Table II)

When we cross tabulated creatinine with hypomagnesemia and used pearson chi square test, it showed significant results (p=0.009) that describes an unequal distribution between both below and above 10mg/dl creatinine level regarding hypomagnesemia. (Table III)

DISCUSSION

There have been some studies to investigate the incidence, prevalence, clinical manifestations, complications and benefit of early diagnosis and treatment of hypomagnesemia in AKI. One such study by Satish et al reported 62% incidence of hypomagnesemia in their study population which is comparable with our study. In our study, among sampled population of 130 patients with acute renal failure, 75 patients (56.7%) had hypomagnesemia. In study by Satish et al total of 50 patients were included and among them 31(62%) had hypomagnesemia. Among that 31 hypomagnesemic patients 23 had symptoms which were treated with magnesium and potassium replacement as they also have hypokalemia and all patients were improved.

Table 1: *Cross Tabulation between Age Groups & Hypomagnesemia*

Parameter	Hypomagnesemia		Total
Age groups	**No**	**Yes**	
Below 45 years	33	29	62
45 years & above	22	46	68
Total	55	75	130
Using Pearson Chi square test p = .016 (significant)			

Table 2: *Cross Tabulation between Gender & Hypomagnesemia*

Parameter	Hypomagnesemia		Total
Gender	**No**	**Yes**	
Male	23	44	67
Female	32	31	63
Total	55	75	130
Using Pearson Chi square test p = 0.058 (not significant)			

Table 3: *Cross tabulation between Creatinine Group & Hypomagnesemia*

Parameter	Hypomagnesemia		Total
Creatinine Group	**No**	**Yes**	
Below 10 mg/dl	29	56	85
10 mg/dl & above	26	19	45
Total	55	75	130
Using Pearson Chi square test p = 0.009 (significant)			

Major symptoms reported were paresthesia, irritability, agitation, dysarthria and vertigo.[10] Another study by Raveendra et al shows prevalence of hypomagnesemia in AKI was 53 % at day one of admission which is consistent with our findings.[14] While another study by Alves et al showed almost equal prevalence of hypomagnesemia in critically ill patients regardless of renal failure (47% with AKI versus 62% in non AKI with P = 0.36) which is inconsistent with our study but that study showed that low magnesium was an independent risk factor of mortality in patients of AKI and it was observed that hypomagnesemia was higher in patients who didn't recovered from acute renal insult.[15] One of the other available studies by Cheungpasitporn et al which was a single center retrospective study to determine the correlation of hypomagnesemia and hypermagnesemia with the risk of AKI. It was a comparatively large study which has included 9241 patients. It demonstrated the inverse relationship of magnesium with incidence of acute renal failure) i.e. the incidence of AKI was lowest when the serum magnesium was within normal ranges and incidence of AKI was higher both with hypomagnesemia and hypermagnesemia.[16] Another study by Santos et al which was conducted in AIDS patients also consistent with the previous mentioned results in which hypomagnesemia was found an independent risk factor for non-recovery of AKI. Other factors found that were risk factors for non-recovery of AKI were need for dialysis, sepsis and dehydration.[17] So, significance of our study was well established in terms of finding hypomagnesemia in AKI patients and correcting it to improve the renal outcomes in AKI patients.

Age of our study population ranged from 23 to 70 years with mean of 45.9 ± 12.9 years), 62 patients (47.7%) were below 45 years and 68 patients (52.3%) were either 45 years of age or above. When we cross tabulated age group with hypomagnesemia and used Pearson chi square test, it showed significant results (p=0.016). 45 years & above age group was found more prone to develop hypomagnesemia during acute renal failure. It implies that more focus should be placed in older patients and they should be screened.

67 patients (51.5%) were male and remaining 63 patients (48.5) were female. On cross tabulating hypomagnesemia with gender, results came up statistically non-significant. It implies that both male and female are equally prone to development of hypomagnesemia. Similarly, when we cross tabulated creatinine with hypomagnesemia and used Pearson chi square test, results were significantly different in two groups. A high baseline serum creatinine shows more risk of having hypomagnesemia.

Limitations of current study includes single center study and small sample size.

CONCLUSION

Hypomagnesemia is an under recognized electrolyte abnormality associated with AKI. Early identification can help prevent the renal complications associated with especially the worsening if GFR.

Magnesium levels can be made a part of initial AKI investigation protocol, for prompt recognition and treatment.

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VACCINATION STATUS AND CAUSES OF NON-IMMUNIZATION IN A SUBGROUP OF THE POPULATION

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Abstract

Objective: to access the vaccination status in a subgroup of children visiting a tertiary care hospital for any reason and know about the reasons for non-immunization.

Methodology: This cross-sectional study was conducted in the Paediatric Department of Lahore General Hospital from Jan 2017 to Dec 2017. Children were selected according to inclusion criteria, and pre-designed proformas were filled. The proforma include patient biodata, Parent education (labeled educated who has primary or above qualification), working status, Vaccination status, either fully vaccinated according to EPI schedule, partly (who missed one or more than one vaccine) or unvaccinated.

Results: The mean age of the children was 6.20 (SD ± 4.33) years. 58% were male, and 42% were females. 75% of children were completely vaccinated; partly, children were 17%, and 8 % were unvaccinated. Parent's education has a statistically significant impact on their children's vaccination status. The most common reasons for non-vaccination or partial vaccination were negligence, unawareness and lack of knowledge about its importance. (Unaware 24.5 %, negligence 33%, did not consider it important 7.5%, think vaccination is harmful 5%, waiting for mobile team 8 %, no nearby vaccination centre 7.5%, family problems 7%, other issues7.5 %).

Conclusion: vaccination status is still very unsatisfactory in Pakistan. Reinforcement of vaccination importance and public awareness is strongly needed.

Keywords: Vaccination status, non-utilization of vaccination, EPI, Pakistan.

Immunization in children is of paramount importance for a healthy society and nation. It is considered the most effective way to save millions of lives from life-threatening but preventable diseases. The EPI (expanded program of immunization) was started by WHO in 1974 against six diseases tuberculosis, polio, diphtheria, pertussis, tetanus and measles. In Pakistan, this program was started in 1978 with six vaccinations. Vaccinations against hepatitis B and Hemophilus influenza were included in 2002, and the pneumococcal vaccine was added to the program in 2015, followed by the Rota vaccine in 2017.[1]

According to EPI, all children are inoculated at birth with BCG (Bacille Calmette Guerin) vaccine and the oral polio vaccine. Further immunization visits are at 6, 10 and 14 weeks when DTP, Hib, HBV, Polio vaccine and Pneumococcal vaccine are given, followed by the measles vaccine at nine months.[2]

When EPI was started in 1974, the coverage was less than 5%, which gradually improved to 74% until 1998. As a result of global campaigning, the coverage against pertussis and diphtheria has increased to around 83% by 2013. Due to effective immunization, 2-3 million childhood deaths are prevented worldwide.[3] The number of deaths by measles has also reduced by 74%. Despite this global campaigning, around 22.6 million children worldwide are still not vaccinated, which is highest in developing countries. More

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than 20% of children worldwide are not fully vaccinated, and there are around 3 million deaths every year from vaccine-preventable diseases.[4]

In Pakistan, though the routine reporting from provinces regarding vaccination indicates overall coverage of about 80% but according to Pakistan demographic household survey 2012-2013, the overall national average of vaccination coverage is only 53.8% with Punjab 65.6%, KPK 52.7%, Sindh 29.1% and Balochistan 16.4% showing that coverage of vaccination is poor, which results in a significant number of preventable deaths.[5] Pakistan is a country with the highest rates of death in children due to vaccine-preventable diseases. One child out of 11 born children dies before turning five years, and about half of all the deaths in children are below 5-years, compared with 8-10% of all the childhood deaths in developed countries.[6] According to an immunization coverage survey, 1 in every five children is not immunized, and in many rural areas, 2 out of 3 children are not vaccinated. The coverage of vaccines in Pakistan is highest for BCG, DTP and HBV and lowest for polio. Pakistan is lagging behind the regional countries in terms of vaccination coverage.[7] Factors mainly responsible for poor vaccination status in our population are poor education of parents, poor socioeconomic status, unemployment, lack of awareness about vaccines' benefits, social myths about vaccines, and poor access to vaccination centers.[8, 9] The rationale of the study is to determine the vaccinations status of children presenting to hospital with different problems and to determine the causes of vaccination failure by looking at the different factors, which will provide data to healthcare providers to take appropriate steps that would improve immunization coverage and make special immunization arrangements for unvaccinated children presenting in hospital. This study aimed to access the vaccination status in a subgroup of children who were visiting a tertiary care hospital for any reason and knowing about the reasons for non-immunization.

Inclusion criteria: children from 15th month of age to 12 years were included in the study

Exclusion criteria: Those children were excluded from the study whose parents/ guardians were not sure about vaccination status and those who did not gage consent.

Study Design: Cross-sectional study

Sampling technique: non-probability consecutive sampling.

METHODOLOGY

It was a cross-sectional survey that was conducted at the pediatric department of Lahore General Hospital. Permission was taken from the hospital ethical committee. During the study period, children who visited the hospital were selected according to inclusion criteria, and constant was taken. Parents have explained the reason for questioning, and proformas were filled. The proforma was designed that included patient biodata, Parents' education (labeled educated who has primary or above qualification), working status, Vaccination status, either fully vaccinated according to EPI schedule, partially (who missed one or more than one vaccine) or unvaccinated. All the data was entered on spss version 20 and analyzed. Numerical data were presented as mean ± standard deviation (SD), and non-numerical data were expressed as frequency percentages. Chi-Square was applied where applicable. The level of significance was considered $p < 0.05$.

RESULTS

The mean age of the children in our study was 6.20 (SD ± 4.33) years. 58% were male, and 42% were females. Regarding the educational status of parents, 49% of mothers and 59% of fathers were educated. Only 13% of children in our study had working mothers. Children who have completed their immunization according to EPI were 748, that was 75%.17% of the children were partly vaccinated while unvaccinated children were 8 %(Figure 1). Males were relatively more completely vaccinated than females that were 75% vs. 74%. Unvaccinated females were 19% compared to males in whom 16% were non-immunized, but the p-value calculated for gender

difference was not significant. Parents' education status was noted to impact immunization status significantly, as 86% of children of educated mothers were vaccinated, while only 64% of children of uneducated mothers were vaccinated. p-value calculated was < 0.001. Similarly, the father's education status has influenced the child vaccinated as educated fathers children were 83% vaccinated compared to uneducated fathers children that were 63% vaccinated. p-value calculated was < 0.001(Table 1).The difference was also noted in the vaccination status of those with working mothers, 73% vs. 75%, but it was not statistically proved (Table 2).

The most common reason was either the parents were unaware of the program or were ignorant of getting their children vaccinated. 33% were negligent, while 24% were unaware. 7.5% considered it unimportant rather, 5% of parents consider immunization harmful for their children. Children who missed the vaccination because the mobile team did not visit their house were 8%, while the 7.5 % were from the outreach area where there was no vaccination center, or it was not in their knowledge. 7% of mothers reported that they could not vaccinate their children because of family issues, 7.5% has miscellaneous issues (Table 3).

Table 1: *Parents' Education and Immunization Status Relationship*

Education status of parents	Immunization status of children			Total	p-value
	Vaccinated	Partially vaccinated	Un vaccinated		
Educated mothers	423	53	13	489	<0.001
Un-Educated mothers	325	120	66	511	
Educated fathers	487	72	25	584	<0.001
Un-Educated fathers	261	101	54	416	

Table 2: *Mother's job and immunization status relationship.*

Job status	Immunization status			Total	p-value
	Vaccinated	Partially vaccinated	Un-vaccinated		
Working mother	95	24	11	130	>0.001
House wife	653	149	68	870	

Table 3: *Reasons for non/partial immunization*

Reason for non/ Partial immunization	No of patients	Percentage
Un aware	61	24.5%
Negligence	83	33%
Don't think its important	19	7.5%
Thinks its harmful	13	5%
Waiting for mobile team	20	8%
No nearby vaccination centre	19	7.5%
Family issues	18	7%
Other issues	19	7.5%

DISCUSSION

Non-immunization and incomplete vaccination are very sensitive, and one of the major issues regarding child health in Pakistan. WHO and UNICEF estimates of national immunization coverage in Pakistan show no remarkable improvement in immunization coverage in the last decade.[10] In our study, immunization coverage recorded is 74.8%. Other studies and surveys were done in Pakistan show almost similar coverage in Punjab, Pakistan.[11,12] Data collected in our study is from a big city of Punjab, Lahore and immunization coverage here is also not satisfactory, and condition in peri-urban areas is more disappointing.[13]

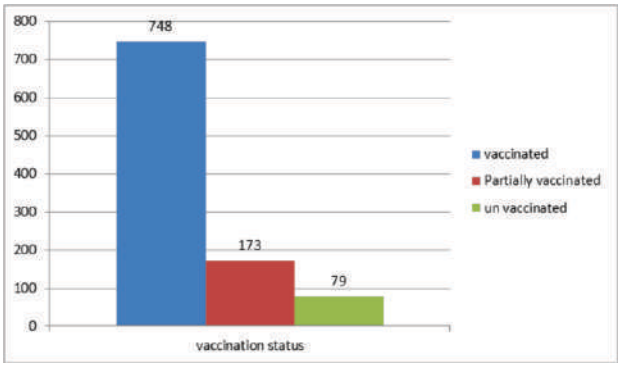

Figure 1: *Vaccination Status of Children*

In 2011, Asif Raza Khawaja et al. concluded in their study that vaccination coverage is 75%. The state is notably low than the percentage concluded after the 2008 survey, which was 85%.[14]

It's very unsatisfactory that we are far behind our development goals. The factors responsible for such a low vaccination coverage must be addressed. According to our study results, literacy has a significant

impact on immunization. A statistically significant difference was noted in the vaccination status of children of educated vs. uneducated mothers (86% vs. 64%). Similarly, the father's educational status positively impacts their children's vaccination status (Table 1). So improving the literacy rate will automatically increase the immunization coverage. Other studies also favor that educated parents are better aware of immunization, schedule, and importance than the uneducated ones.[15]

The educational status of parents has a positive impact on completing the vaccination schedule of their children. There can be many factors associated with education in this regard. In one study in rural Sindh, they emphasized that vaccination cards are too small and healthcare professionals' handwriting about the next date for vaccination is difficult to read on many occasions. So educated people can have some idea in general and anticipate the next dose but people with low educational status have only this card as a source of information. They intervened in this aspect and redesigned the vaccination card with a more prominent next dose date. This study showed very promising results. A randomized controlled trial in rural Pakistan showed that only the revised vaccination card and maternal education significantly improved the adherence to the vaccination schedule.[16]

Another factor associated with education is general motivation and awareness about diseases against which EPI vaccination is available. Educated parents know this from other sources, but low-educated people have only gotten knowledge from EPI staff. Due to their limitations, this staff has not effectively sensitized the population about its importance. So, in addition to improving parents' educational status, specific training of EPI about counseling may help achieve the desired results.[16]

Working mothers' children were also less vaccinated than homemakers, but it was not statistically proved. It may be the reason that only 13% of the mothers in our study were working women (Table 2).

Regarding the reasons for non-immunization or partial vaccination, most of the issues are related to poor awareness about immunization, its schedule and importance. 33% were negligent about their child vaccination, and 24% were unaware of either immunization or its complete schedule. 5% of the parents in our study think vaccination is harmful to their child. Misconceptions like this must be addressed and corrected at every level. In 2007 a study was conducted in Agha Khan University Karachi about the knowledge, attitude, and practice regarding immunization and suggested that the education and motivation for immunization are strongly needed.[17]

In our study, 8 % of children missed the vaccination because the mobile team did not visit their house, so the mobile teams must be made more efficient and regular. Other causes were related to social reasons that led the children unimmunized.

Overall, 70% of the causes of immunization failure in our study were related to poor public awareness and misconceptions. Public awareness campaigns by the government and electronic and social media are the need of time and will hopefully improve the vaccination coverage.

To improve vaccination coverage, a comprehensive policy regarding education, health and socioeconomic aspect is required. This study was conducted in a tertiary care hospital in a big city, and almost all of the children belong to poor socioeconomic status. A community-level survey with a large sample size with more elaboration of causes of non-immunization is needed.

CONCLUSION

Non-utilization of vaccination is still a major health-related threat to Pakistani children that need the kind attention of government and non-government bodies. The majority of the reasons for this are poor awareness that will help us reduce our under-five mortality.

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ASSESSMENT OF DENTISTS' KNOWLEDGE ABOUT ACUTE DENTAL PAIN MANAGEMENT IN PREGNANT FEMALES

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Abstract

Background: Pregnancy is a unique period in a woman's life. During pregnancy, altered level of progesterone and estrogen enhances the patency of the oral vascular structures and decrease immunocompetence, hence enhancing the inflammation tendency. Pregnant females are more vulnerable to dental caries, tooth mobility, erosion and gingivitis, and hence should get proper oral healthcare. Also, the pregnant females mostly need dental emergency services because of acute dental pain episodes.

Objective: The objective of the study is to assess dentists' knowledge about acute dental pain management in pregnant females.

Methodology: It was analytical cross-sectional study in which 150 dentists from Sheik Zayed Hospital, Lahore were included. Non-probability convenient sampling technique was used.

Results: Among 150 dentists, 58.0% were females and the mean age was 37.58 ± 4.3 years. 32.0% dentists had excellent knowledge and 38.0% had good knowledge while 30.0% dentists had poor knowledge regarding acute dental pain management among pregnant women. There was significant association ($P<0.05$) of age and experience with knowledge level of dentists while insignificant association ($P>0.05$) of gender and education with knowledge level of dentists.

Conclusion: Study concluded that among dentists, knowledge was found satisfactory (correct knowledge 70.0%) but there is further need to improve their knowledge level because 30.0% dentists had poor knowledge about management of dental pain among pregnant women.

Key Words: Assessment, dentist, acute dental pain, management, pregnancy

Pregnancy is a unique period in a woman's life.[1] It is one of the physiological conditions due to several changes in woman entire body as well as oral cavity.[2-4] During pregnancy, altered level of progesterone and estrogen enhances the patency of the oral vascular structures and decrease immunocompetence, hence enhancing the inflammation tendency. Pregnant females are more vulnerable to dental caries, tooth mobility, erosion and gingivitis, and hence should get proper oral healthcare. Also, the pregnant females mostly need dental emergency services because of acute dental pain episodes.[5,6] A study conducted in Pakistan reported that during pregnancy the dental pain prevalence was 20.7%.[7] It is the very common indication for which patients seek the dental treatment.[8]

The treatment of dental problems during pregnancy has barriers and limitations for the patient and the dentist. Pregnant women often do not usually follow the treatment due to fear and concern of dental treatment as well as low level of knowledge about dental problems, and incorrect perception of dental treatments that affect fetal growth.[9,10] Despite the ample evidence concerning the safety of dental procedures during pregnancy, several oral health professionals still have some fear of treating these patients. Lack of knowledge and unpreparedness among dental surgeons are the main causes for not treating these patients.[11]

Therefore, it is important that dentists should

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have appropriate knowledge and attitude towards the endodontic treatments for women during pregnancy.[12] In a Nigerian study, 91.8% dentists had firm belief that RCT (root canal treatment) is normally safe during pregnancy and 77% believed that local anesthetic along with the epinephrine is secure, while 57.4% dentists believed that during pregnancy radiographs are safe. The research also highlighted that knowledge level differs significantly in different specialties.[13]

In another research carried out among Australian dentists, 99% were agreed that pregnant females should obtain dental examinations; though, only 22 percent had good knowledge regarding pregnant females' treatment in the dental clinics. Actually, the dentists who had inadequate knowledge mostly delayed the dental appointments from medical physicians prior to providing treatment. Given that 95.7 percent requested further information regarding treatment of pregnant females which shows that there is need to enhance dentists' knowledge regarding pregnant female treatment in their dental clinics.[14]

A study of Pakistani dentists found that 86.5 percent dentists were agreed to give dental treatment services to the pregnant females, 35.3 percent considered 2nd trimester as an optimum time for taking radiograph, 33.5 percent advised amoxicillin, 76.7 percent believed paracetamol is safe for pregnant females, 54 percent favored local anesthesia along with vasoconstrictor. Among dentists, 43.3 percent refused to provide treatment during any trimester, 46.5 percent said that amalgam usage is safe during the period of pregnancy, 70.7 percent preferred use of composite as well as glass ionomer cement, 34.4 percent preferred second trimester to carry out endodontic treatment and 32.1 percent believed it was secure to carry out at any time while 35.3 percent dentists reported that dental extractions is safe to perform any time. Study results showed lack of knowledge among dentists about dental treatment for women during pregnancy.[15]

In order to help dentists face their anxiety and make right decisions in treating pregnant women, international protocols and guidelines should be followed regarding different dental procedures for example, fillings, RCT, tooth extraction, periodontal treatment, radiographs, medications, local anesthesia and sitting position of pregnant females on dental chair.[16]

There are very few studies carried out in Pakistan that evaluated the level of knowledge of dentists about dental treatment provision during pregnancy. Assessing dentists' knowledge towards pregnant women could help create an advanced oral health-care package for pregnant females together with stakeholders in maternal health-care, which is obligatory for dentists working in Pakistan. This study is carried out to assess dentists' knowledge about acute dental pain management in pregnant females.

METHODOLOGY

It was analytical cross-sectional study in which 150 dentists from Sheikh Zayed Hospital, Lahore were included. Non-probability convenient sampling tech-nique was used. Study included both male and female dentists, aged 20-60 years, with any qualification and clinical practice. Consultants, pregnant dentists and not practicing were excluded from study.

Questionnaire was made which comprised demographic variables such age, gender, education, experience and questions related to assessment of knowledge of dentists regarding management of acute dental pain in pregnant females. Excellent knowledge was measured if correct response rate was >80%, good knowledge equal to 60%, while poor knowledge was measured if the correct response rate below 60%.

Data was collected through questionnaire which was entered and statistically analyzed using SPSS 25.0. As descriptive statistics, data was analyzed to obtain mean+SD scores. For inferential statistics, chi-square test was utilized to know the frequencies of responses and significance of chi-square output was taken as $P \leq 0.05$.

RESULTS

Table-1 asserts that among 150 dentists, 19 (12.7%) were upto 30 years old, majority 126 (84.0)

was 31-50 years old and only 5 (3.3%) dentists were above 50 years old. The mean age of the dentists was 37.58 ± 4.3 years.

Among 150 dentists, 63 (42.0%) were males while 87 (58.0%) were females.

Result shows that majority 127 (84.7%) of the dentists were graduate while only 23 (15.3%) were postgraduate.

Out of 150 dentists, 21 (14.0%) had upto 5 years experience, mainstream 122 (81.3%) had 6-10 years experiences and only 7 (4.7%) dentists had more than 10 years experience.

Table-2 highlights the dentists' knowledge regarding acute dental pain management among pregnant females and found that most of the dentists 129 (86.0%) had knowledge that elective procedures can be carried out in pregnancy, followed by simple extraction can be carried out safely among pregnant women if required 124 (82.7%), non-surgical endodontic treatment can be carried out on pregnant females 123 (82.0%), anesthesia 2% lignocaine along with 1:100,000 adrenaline is safe during pregnancy 123 (82.0%), maintaining the periodontal health is a significant part for healthful pregnancy 120 (80.0%), dentists ever recommended single digital periapical radiograph along with lead apron to the pregnant females 113 (75.3%), dental treatment is advised during all trimesters 98 (65.3%), ever refused the treatment of gravid females 94 (62.7%), antibiotics can be prescribed for pregnant females 86 (57.3%), ibuprofen is safe during third trimester 83 (55.3%) and aspirin can be prescribed for pregnant females 46 (30.7%).

Table 1: *Frequency Distribution of Dentists According to Socio-Demographic Characteristics*

	Frequency	Percentage (%)
Age		
≤30 years	19	12.7
31-50 years	126	84.0
>50 years	5	3.3
Total	150	100.0
Mean ± SD	37.58 ± 4.3	
Gender		
Male	63	42.0
Female	87	58.0
Total	150	100.0
Education		
Graduate	127	84.7
Postgraduate	23	15.3
Total	150	100.0
Experience		
≤5 years	21	14.0
6-10 years	122	81.3
>10 years	7	4.7
Total	150	100.0

Table 2: *Frequency Distribution of Dentists According to knowledge about Acute Dental Pain Management in Pregnant Females n=150*

Assessment of dentists' knowledge	Yes	No
Is the dental treatment advised during all trimesters	98 (65.3%)	52 (3.7%)
Have you ever refused the treatment of gravid females	94 (62.7%)	56 (37.3%)
Can the elective procedures be carried out in pregnancy	129(86.0%)	21 (14.0%)
Do you carry out non-surgical endodontic treatment on pregnant females	123(82.0%)	27 (18.0%)
Can a simple extraction be carried out safely among pregnant women if required	124(82.7%)	26(17.3%)
Is anesthesia 2% lignocaine along with 1:100,000 adrenaline safe during pregnancy	123(82.0%)	27(18.0%)
Can the antibiotics be prescribed for pregnant females	86(57.3%)	64(42.7%)
Can the aspirin be prescribed for pregnant females	46(30.7%)	107(71.3 %)
Is the ibuprofen safe during third trimester	83 (55.3%)	67 (44.7%)
Is maintaining the periodontal health a significant part for healthful pregnancy	120(80.0%)	30 (20.0%)
Have you ever recommended single digital periapical radiograph along with lead apron tothe pregnantfemales	113(75.3%)	37 (24.7%)

Table-3 exhibits that out of 150 dentists, 48 (32.0%) had excellent knowledge and 57(38.0%) had good knowledge while 45 (30.0%) had poor knowledge regarding acute dental pain management among pregnant women.

Table 3: *Frequency Distribution of Dentists According to Knowledge Level*

	Frequency	Percentage (%)
Excellent	48	32.0
Good	57	38.0
Poor	45	30.0
Total	150	100.0

Table-4 shows significant association (P<0.05) of age and experience with knowledge level of dentists

while insignificant association (P>0.05) of gender and education with knowledge level of dentists.

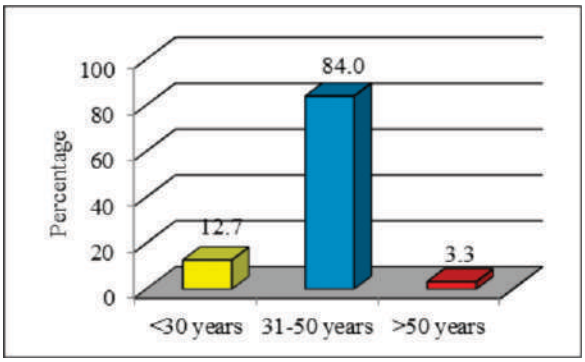

Figure-1: *Frequency Aistribution of Dentists according to Age*

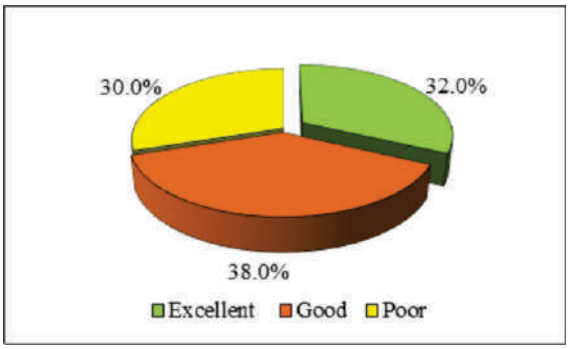

Figure-2: *Frequency distribution of dentists according to knowledge level*

Table 4: *Association between Socio-Demographic Characteristics and knowledge Level of Dentists*

Socio-demographic characteristics	Knowledge level			Total	P-value
	Excellent	Good	Poor		
Age					
≤30 yrs	9 (6.0%)	8 (5.3%)	2 (1.4%)	19(12.7%)	
31-50 yrs	36 (24.0%)	48 (32.0%)	42 (28.0%)	126(84.0%)	0.003
>50 yrs	3 (2.0%)	1 (0.7%)	1 (0.7%)	5 (3.3%)	
Total	48 (32.0%)	57 (38.0%)	45 (30.0%)	150(100.0%)	
Gender					
Male	18 (12.0%)	22 (14.7%)	23 (15.3%)	63 (42.0%)	
Female	30 (20.0%)	35 (23.3%)	22 (14.7%)	87 (58.0%)	0.121
Total	48 (32.0%)	57 (38.0%)	45 (30.0%)	150(100.0%)	
Education					
Graduate	38 (25.3%)	50 (33.4%)	39 (26.0%)	127(84.7%)	
Post-graduate	10 (6.7%)	7 (4.6%)	6 (4.0%)	23(15.3%)	0.143
Total	48 (32.0%)	57 (38.0%)	45 (30.0%)	150(100.0%)	
Experience					
<5 yrs	9 (6.0%)	11 (7.3%)	1 (0.7%)	21 (14.0%)	
6-10 yrs	35 (23.3%)	45 (30.0%)	42 (28.0%)	122(81.3%)	0.001
>10 yrs	4 (2.7%)	1 (0.7%)	2 (1.3%)	7 (4.7%)	
Total	48 (32.0%)	57 (38.0%)	45 (30.0%)	150 (100.0%)	

DISCUSSION

During pregnancy females are required dental emergency services because of acute dental pain episodes. Keeping in mind this problem, present study was carried out to evaluate the dentists' knowledge about acute dental pain management among pregnant females. To acquire appropriate outcomes, 150 dentists were included in the study and found that majority (84.0%) was 31-50 years old while 12.7% and 3.3% dentists were upto 30 and above 50 years old, respectively. The mean age of the dentists was 37.58 ± 4.3 years but the findings of a study conducted by Nasir and coworkers (2017) showed different scenario that mean age of the dentists was 27.69±3.2 year.[15] In our study female dentists were in majority (58.0%) while a similar study carried out by Wali and associates (2016) also reported comparable results that 57.0% were female dentists.[17]

Study revealed that most of the dentists (84.7%) were graduates and only 15.3% had done their post-graduation. The results of a study undertaken by George and collaborators (2017) also confirmed that majority (66.9%) of the dentists were graduates.[14]

Adequate experience of dentists plays a significant role in the management of dental pain among pregnant women. It is important to mention that mainstream (95.3%) had upto 10 years experience and 4.7% dentists had >10 years experience but Nasir and coworkers (2017) reported in their study that 9.8% dentists had above 10 years experience.[15]

When the knowledge of dentists was assessed regarding acute dental pain management among pregnant females, study disclosed that most of the dentists (86.0%) were aware that elective procedures can be carried out in pregnancy, followed by simple extraction can be carried out safely among pregnant women if required (82.7%), non-surgical endodontic treatment can be carried out (82.0%), anesthesia 2% lignocaine along with 1:100,000 adrenaline is safe during pregnancy (82.0%), maintaining the periodontal health is a significant part for healthful pregnancy (80.0%), dentists ever recommended single digital periapical radiograph along with lead apron to the

pregnant females (75.3%), dental treatment is advised during all trimesters (65.3%), ever refused the treatment of gravid females (62.7%), antibiotics can be prescribed for pregnant females (57.3%), ibuprofen is safe during third trimester (55.3%) and aspirin can be prescribed for pregnant females (30.7%). The findings of a study done by Umoh and Azodo (2013) showed encouraging results that 93.7% dentist had knowledge that dental treatment can be provided to females during pregnant.[18] A similar study performed by Prashaanthi and Roy (2017) asserted that mainstream (92.6%) of dentists prescribed drugs for pregnant females.[19] In a recent study AlShurman et al. (2021) confirmed that 92.9% dentists provided endodontic treatment to females during pregnancy.[16] The results of a study carried out by George and partners (2017) confirmed that significant majority (90.3%) of dentist was found comfortable while performing tooth extraction in pregnant women.[14] Tantradi and Madanshetty (2013) asserted in their study that 80.0% dentists had knowledge about the usage of local anesthetics.[20] In a study Jayabalan and Muthusekhar (2020) elucidated that during pregnancy 76.0% dentists prescribed antibiotics[21] while Aboalshamat and teammates (2020) indicated that 31.6% dentists had knowledge that ibuprofen and aspirin are safe for women in pregnancy.[12] A study undertaken by Wali and associates (2016) stated that 92.0% dentists were aware that preventive measures are taken for radiographs among pregnant females.[17] Another study performed by Razi and fellows (2011) described that 92% dentists had knowledge about the need of lead aprons use during radiography.[22]

It was found during study 32.0% dentists had excellent knowledge, 38.0% had good knowledge and 30.0% dentists had poor knowledge regarding acute dental pain management among pregnant women. Virtually the findings of a study carried out by George and collaborators (2017) are comparable with our results who reported that 68.6% dentists had correct knowledge.[14] But results of the studies conducted by Nasir et al.[15] and AlShurman et al.[16] highlighted that dentists had inadequate knowledge regarding management of acute dental pain among females during pregnancy.

Study also assessed the association between socio-economic characteristics and knowledge level of dentist, result showed significant association ($P<0.05$) of age and experience with knowledge level of dentists while insignificant association ($P>0.05$) of gender and education with knowledge level of dentists. But the results of a study undertaken by Mehdipour and comrade (2017) demonstrated statistically insignificant association ($P>0.05$) for age, education and experiences with dentists' knowledge level.[23] A study conducted by AlShurman et al. (2021) also confirmed insignificant association between gender of dentists and their knowledge level.[16]

CONCLUSION

Study concluded that among dentists, knowledge was found satisfactory (correct knowledge 70.0%) but there is further need to improve their knowledge level because 30.0% dentists had poor knowledge about management of dental pain among pregnant women. Further studies are required to be conducted on large scale to assess the dentists' knowledge.

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MEAN SERUM CALCIUM LEVELS AND LIPID PROFILE IN PATIENTS WITH GALLSTONE DISEASE

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Abstract

Background: Gallstone disease is one of the most common gastrointestinal disorders, prevalent in about 10–15% of adults in the developed countries. Most of the patients with this disease are asymptomatic. The role of serum lipids in the etiology of cholelithiasis is very important and in cholesterol gallstones serum lipids are altered which is suggestive of metabolic syndrome. The objective of this study was to find mean serum calcium and lipid profile levels in patients with gallstone disease.

Methodology: It was a cross sectional study carried out on patients having gallstone disease, presenting in Surgical Unit I, Department of Surgery, Jinnah Hospital, Lahore. Serum levels of calcium were carried out on 5 ml venous sample at the time of inclusion into study. Serum lipid profile was done on 5 ml venous sample after an overnight fast of 8 hours. The samples were sent to the hospital laboratory of Jinnah Hospital to control bias. All the data was entered in predesigned proforma. Outcome variables such as serum calcium and lipid profile levels including cholesterol, triglycerides, HDL, LDL and VLDL were recorded.

Results: In our study, 60 patients with gallstone disease were enrolled. 73.33% (n=44) were between 20-40 years of age while 26.67% (n=16) were between 41-70 years of age, mean age was calculated as 38.32± 8.64 years, 23.33% (n=14) were male and 76.67% (n=46) were females. Mean variables of the study were calculated as 9.2±0.55 calcium, 195.83±52.03 for cholesterol, 151.47±85.05 for triglycerides, 42.93±8.74 for HDL, 121.7±5.47 for LDL, 21.53±17.21 for VLDL and 20.76±1.59 for BMI.

Conclusion: We concluded that mean serum calcium level and lipid profile is increased in patients with gallstone disease.

Key Words: Gallstone disease, mean serum calcium and lipid profile levels

In western societies and Pakistan more than 70% of gallstones are composed primarily of cholesterol, either pure or mixed with pigment, mucoglycoprotein, and calcium carbonate. Pigment stones, which are more common in Asians, account for the rest of gallstones.[1] The most accurate and non-invasive method to detect gallstones is the abdominal ultrasonography which carries more than 95% sensitivity and specificity.[2]

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There are certain independent/non-modifiable risk factors for the gallstone disease such as increasing age, race, female gender and family history.[3] Dietary risk factors like high caloric, high cholesterol, high fat and low fiber diet are however modifiable and therefore can be the basis for preventive measures against gallstone disease.[3] The association of dietary factors with gallstones has been questioned in various studies.

Channa et al.[4] in 2012 showed that serum calcium level was raised among gallstone patients (13.1±4.63). Singh et al.[5] in 2013 showed that patients with gallstones had high serum Total Cholesterol (17.00±7.99), Triglycerides (142.53±6.09),High Density Lipoprotein (HDL; 4.39± .89), Low Density Lipoprotein (LDL; 28.51±1.21).

The high incidence of obesity and gallstone disease and also the nature of the gallstones commonly encountered in our population advocate the need for new research in Pakistani population. The purpose of this study is therefore to find mean serum level of calcium and lipid profile in Pakistani patients with gallstone disease. If we find high mean levels in this study then the results may be utilized to formulate guidelines for early identification of the people who are at greater risk and preventive measures to reduce the economic burden and overall morbidity of the patients with gallstone disease in our population.

METHODOLOGY

Patients with gallstone disease of any duration who presented in Surgical Unit I, Department of Surgery, Jinnah Hospital, Lahore from 1st Oct 2020 till 31st Mar 2021, were included in to the study. Patients with obstructive jaundice (ALP>300 mg/dl), patients with renal failure (creatinine > 1.2 mg/dl and liver disease (AST > 40 IU, ALT > 40 IU) or patients of pancreatitis (Amylase >200mg/dl) and cardiac disease (on history or previous medical record) were excluded. Written informed consent and detailed history was taken from each patient. Demographic details of the patient such as age, gender, address and BMI was recorded. Serum levels of calcium were carried out on 5 ml venous sample at the time of inclusion into study. Serum lipid profile was done 5 ml venous sample after an overnight fast of 8 hours. The samples were sent to the hospital laboratory of Jinnah Hospital to control bias. All the data was entered in predesigned proforma. Outcome variables such as serum calcium and lipid profile levels including cholesterol, triglycerides, HDL, LDL and VLDL were recorded. All the data was entered into SPSS version 18. Quantitative variables such as age and serum levels of calcium, cholesterol, triglycerides, HDL, LDL, and VLDL, BMI were presented as mean±SD. Qualitative variables such as gender were presented as frequency and percentage. Data was stratified for age, gender, BMI and duration of disease to deal with effect modifiers. Post stratification t-test was applied. P-value < 0.05 as level of significance.

RESULTS

A total of 60 cases fulfilling the inclusion/ exclusion criteria were enrolled to find mean serum calcium and lipid profile levels in patients with gallstone disease. Patients were distributed according to age of the patients, it shows that 73.33% (n=44) were between 20-40 years of age while 26.67% (n=16) were between 41-70 years of age, mean±sd was calculated as 38.32 ± 8.64 years. Gender distribution of the patients shows that 23.33% (n=14) were male and 76.67% (n=46) were females. Mean variable of the study were calculated as 9.2±0.55 calcium, 195.83±52.03 for cholesterol, 151.47±85.05 for triglycerides, 42.93±8.74 for HDL, 121.7±5.47 for LDL, 21.53±17.21 for VLDL and 20.76±1.59 for BMI. (Table 1)

Table 1: *Mean Variables of The Study (n=60)*

Variables	Mean	SD
Calcium	9.26	0.55
Cholesterol	195.83	52.03
Triglycerides	151.47	85.05
HDL	42.93	8.74
LDL	121.7	5.47
VLDL	21.53	17.21
BMI	20.76	1.59

Table 2: *Stratification for Age (n=60)*

Variables	20-40		41-70		P value
	Mean	SD	Mean	SD	
Calcium	9.23	0.57	9.09	0.51	0.15
Cholesterol	203.30	46.59	188.0	64.89	0.31
Triglycerides	152.57	86.47	148.44	83.72	0.86
HDL	42.95	8.10	42.88	10.60	0.97
LDL	141.36	28.41	143.54	26.77	0.56
VLDL	35.04	17.05	29.71	17.60	0.36

Table 3: *Stratification for Gender (n=60)*

Variables	Male		Female		P value
	Mean	SD	Mean	SD	
Calcium	8.89	0.45	9.38	0.54	0.003
Cholesterol	183.21	40.09	204.11	54.67	0.19
Triglycerides	148.86	56.22	152.26	92.57	0.89
HDL	38.36	10.58	44.33	7.70	0.02
LDL	139.48	21.58	141.57	22.71	0.61
VLDL	29.44	9.49	34.23	18.92	0.47

The data was stratified for age, gender, BMI and duration of disease. (Table 2-5).

Table 4: Stratification for Bmi (n=60)

Variables	17-22		>22		P value
	Mean	SD	Mean	SD	
Calcium	9.25	0.46	9.27	0.64	0.84
Cholesterol	187.31	43.39	210.60	57.64	0.08
Triglycerides	149.79	50.29	153.03	108.91	0.88
HDL	43.83	8.61	42.10	8.92	0.44
LDL	137.21	19.43	142.86	21.64	0.74
VLDL	28.43	6.98	38.61	23.36	0.06

Table 5: Stratification for Duration of Disease

Variables	1-3 years		>3 years		P value
	Mean	SD	Mean	SD	
Calcium	9.24	0.59	9.43	0.19	0.38
Cholesterol	196.82	54.32	214.00	32.67	0.39
Triglycerides	148.15	90.12	173.00	34.53	0.44
HDL	43.25	9.28	40.88	3.31	0.47
LDL	133.24	14.25	138.35	20.44	0.44
VLDL	33.03	18.95	33.57	4.50	0.94

DISCUSSION

Gallstone disease is one of the most common gastrointestinal disorders, known to occur in approximately 20% of healthy individuals. The prevalence of the disease is more than double in females than in males and increases with age in both genders, reaching approximately 30% at the age of 70 years.[6] Most of the patients with this disease are asymptomatic. The role of serum lipids in the aetiology of cholelithiasis is very important and in cholesterol gallstones serum lipids are altered which is suggestive of metabolic syndrome.[7]

In our study, 73.33% patients (n=44) were between 20-40 years of age while 26.67%(n=16) were between 41-70 years of age, mean age was calculated as 38.32± 8.64 years, 23.33%(n=14) were male and 76.67% (n=46) were females. Mean variable of the study were calculated as 9.2±0.55 calcium, 195.83±52.03 for cholesterol, 151.47±85.05 for triglycerides, 42.93± 8.74 for HDL, 121.7±5.47 for LDL, 21.53±17.21 for VLDL and 20.76±1.59 for BMI.

Channa et al.[8] in 2012 showed that serum calcium level was raised among gallstone patients (13.1±4.63). Singh et al.[9] in 2013 showed that patients with gallstones had high serum Total Cholesterol (17.00±7.99), Triglycerides (142.53±6.09),High Density Lipoprotein (HDL; 4.39± 0.89), Low Density Lipoprotein (LDL; 28.51±1.21). Similar results were reported by Virupaksha et al.10 in 2011; total cholesterol (224.3 ± 42.4), LDL (139.3 ±23.8), HDL 47.11±5.11), Triglycerides (185.1±27.8). Al saadi and Al-Ardhi in 2012; reported Cholesterol (75.43±35.89), triglycerides (186.63±67.21), HDL (43.83±7.75), VLDL (37.03± 13.45), LDL (192.21±41.38) in patients of gallstone disease.[11]

However no statistically significant difference was recorded by Jindal et al.[12] 2014; Cholesterol (153.28±25.69), triglycerides (142.67±92.73), HDL (49.53±8.75), LDL (105.94±20.44). Similar results were achieved previously by Batajoo and Hazra in 2013; Cholesterol (189.3±34.037), triglycerides (130.39 ± 48.538), LDL (113.51± 32.717, p= 0.034), HDL (42.20±3.390), VLDL (26.77±8.939).13 Our findings are comparable, though some of the variables are different from our study.

Channa NA et al.[8] found that lipids elevation in cholelithiasis, seems to play a major contributing role in the pathogenesis of gallstones in females of up to 45 years age. The elevation of serum total cholesterol and TG levels in patients may be due to: Gallstone patients have abnormal secretory mechanism for bile acids and phospholipids, decrease bile acids and phospholipids (which solubilize cholesterol in the bile) will increase cholesterol precipitation.[14] Some of gallstone patients may present with metabolic syndrome which is a cluster of symptoms such as glucose intolerance, high total cholesterol, hyperinsulinemia, increased VLDL and/or total cholesterol, decrease HDL and hypertension which indicate that the metabolic syndrome is one of the risk factors for gallstone disease.[15]

CONCLUSION

We concluded that gallstone disease is associated with some biochemical abnormalities (elevation of total cholesterol, triglyceride, LDL, VLDL, fasting serum glucose level) that may be the cause or the result of gallstone formation.

Conflict of Interest

The author(s) declared no conflict of interest with respect to research, authorship and publication of this article

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PREVALENCE OF MALNUTRITION AND ITS CONTRIBUTING FACTORS AMONG CHILDREN AGED 6-59 MONTHS VISITING JINNAH HOSPITAL LAHORE

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Abstract

Background: Malnutrition is an implicit and substantive cause of several diseases and illnesses. World-wide it is the cause of death in one-third children under the age of 5 years. Most of the children inflicted by malnutrition are residing in the developing countries.

Objectives: To find the frequency of malnutrition and contributing factors of malnutrition among children of age 6-59 months.

Methodology: Cross-sectional type of study done at the Jinnah Hospital, Lahore from November 24, 2018 to May 24, 2019. Written informed consent was obtained from the parents of 195 patients fulfilling inclusion and exclusion criteria from the OPD of Paediatrics Department Jinnah Hospital Lahore after explaining the details of the study and its associated benefits and risks. Information regarding their demographic data was noted in the proforma. Main contributing factors for malnutrition were evaluated from their parents. SPSS v23.0 was used to assess the obtained data.

Results: Age range in this study was from 6 to 59 months. Mean age of child was 33.1±15.6months. Among 195 children, 124(63.6%) were males and 71(36.4%) were females.

Conclusion: Out of 195 children, 97(49.7%) had malnutrition. Contributing factors for malnutrition among 97 malnourished children were illiterate mother 66(68.0%); being the prime factor followed by residence in rural areas 55(56.7%), low income 52(53.6), toilet absent 28(28.9%) and working mother 24(24.7%).

Key Words: Malnutrition, Determinants, Children.

Child malnutrition is a pre-eminent public health problem in almost all the developing countries. According to worldwide data by year 2012 there were 165 million stunted, 99 million underweight, and 51 million wasting in children around the world. Malnutrition causes 3.1 million under-five children deaths annually.[1] Children under 5 years of age are very much vulnerable and prone to the effects of malnutrition. Malnutrition in the initial growing years of a child can endanger the cognitive development and increase the risk of various infections. Consequently, decreasing the quality of life and increasing the risk of death. Malnutrition leads to persistent effects on growth and development of children. It leads to debilitating damaging effects on the mental development and causes preclination towards chronic illnesses later in the life.[2]

All around the world in various studies the causal factors of acute malnutrition among children aged 6–59 months were found to be poverty, lack of education, poor decision making by parents based on their cultural food-fads, insufficient feeding practices, supersized-family, non-exclusive breastfeeding, loose motions, low weight at birth, immunization status, unstable family, poor mother hand sanitization habit and multiple pregnancies.[3] Poverty is the main impul-

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sive force escalating to malnutrition in underdeveloped and developing countries which entails to food insecurity.[4]

Nonetheless, recent studies done in the developing countries show double-burden of malnutrition both due to under nutrition and over nutrition.[5] Poor are also presenting with obesity, and bipartite burden is seen in poor communities.[6] Malnutrition is the foremost and paramount cause of mortality and morbidity in young children across the world; its responsible for 45 percent of all deaths among children under five years of age.[7]

Pakistan is worth a mention as a country with the highest load of malnutrition. Jinnah Hospital Lahore is a tertiary care centre where patients from all parts of the country are being treated. There is insufficient and limited data on malnutrition and its contributing factors in children in local settings , not many studies are available at the time being. This study will help in identifying the prevalence of malnutrition and its various contributing factors. The results of this study will help in improving the nutritional status of under 5 years age children. Henceforth, playing a role in reducing the morbidity and mortality in children.

Malnutrition was considered as weight for height of 70%, presence of bilateral pitting edema and mid upper arm circumference of <115 mm.

Following contributing factors for malnutrition were included:

Low income (<20,000 rupees),

Illiterate mother (no reading and writing),

Residence in rural area/urban area,

Toilet absent (Yes/No),

Working Mother (working ≥36 hours/week)

METHODOLOGY

A cross-sectional type of study was conducted in Pediatrics Medicine Department, Jinnah Hospital, Lahore from November 24, 2018 to May 24, 2019 six months after the approval of synopsis using non-probability consecutive sampling. 195 cases fulfilling the inclusion criteria were selected using non-probability consecutive sampling technique calculated with 95% confidence level, margin of error as 7% and expected percentage of malnutrition as 54% among children of 6-59 months age.[8]

Children of both gender and ages between 6-59 months presenting in pediatrics OPD for routine checkup were part of the study. Children with physical deformities (children without hands because of congenital deformity or with wounds or burns on hands; as cannot obtain mid upper arm circumference accurately in such cases). Patients who were not giving consent were excluded.

Study was started after taking permission from the institutional ethical committee.195 patients were recruited for the study. The details of study and its associated benefits and risks were explained and then written informed consents were taken from the parents / guardian. Interview was taken from the parents in the outpatient department name, age, gender, presence of malnutrition, if malnourished then its contributing factors were noted down in the proforma.

RESULTS

Data from the questionnaire profroma was entered in SPSS version 23.0 for analysis. Numerical variable which includes age was shown as a mean and standard deviation. Qualitative descriptive variables which here imply gender, malnutrition (yes/no,) low income (<20,000 rupees), illiterate mother (no reading and writing), residence in rural area urban area, toilet absent (Yes/No), working mother (working ≥36 hours/ week) were shown as frequencies and percentages. Stratification of the data was done for age and gender of children to sort out the issue of effect modifiers. $p < 0.05$ was taken as statistically significant and after the stratification of variables Chi-square test was applied. Mean age of child was 33.1±15.6 months. Accor-ding to stratification of malnutrition with respect to gender, there was no significant difference between male and female (p=0.839).According to stratifica- tion of malnutrition with respect to age, there was a significant difference among the age groups

Table 1: Prevalence of Malnutrition and Demographic data

Variables n= 195	Frequency	Percentage
Gender		
Male	124	63.6%
Female	71	36.4%
Malnutrition		
Yes	97	**49.7%**
No	98	50.3%
6-12 months	24	12.3%
12-36 months	83	42.6%
36-59 months	88	45.1%

Table 2: Contributing factors of malnutrition among 97 malnourished children

Contributing factors among 97malnourished	Frequency	Percentage
Mothers Education(no reading and writing)		
Illiterate	66	**68.0%**
Literate	31	32.0%
Residential Status		
Rural	55	**56.7%**
Urban	42	43.3%
Distribution of Low income (<20,000rupees)		
yes	52	**53.6%**
no	45	46.4%
Distribution of Toilet absent(yes/no)		
yes	28	**28.9%**
No	69	71.1%
Working mother (**working** ⩾36 hours/week)		
yes	24	**24.7%**
no	73	75.3%

Table 3: Stratification of malnutrition with respect to age groups

Age Groups	Malnutrition		Total	p-value
	Yes	No		
6-12 months	9	15	24	0.035
	37.5%	62.5%	100.0%	
12-36 months	37	46	83	
	44.6%	55.4%	100.0%	
36-59 months	51	37	88	
	58.0%	42.0%	100.0%	
Total	97	98	195	
	49.7%	50.3%	100.0%	

(p=0.035).

DISCUSSION

Malnutrition in children under five years of age is a crucial paramount health issue of utmost concern preliminarily in the developing countries including Pakistan. The results of this study show that almost half of the children (49.7%) had malnutrition.

The results of our study are equivocal with a study in which association of literacy of mothers with malnutrition among children under three years of age in rural area of district Malir, Karachi was studied. In this study stunting (40.75%) was found in 41% children compared to our study where its 49.7% and illiteracy among mothers was found to be 80% compared to 68% in our current study.[9] National Nutritional Survey (2011) labeled 46% stunting in rural areas compared to 49.7 % in ours. The findings of present study are synchronous with a study done in Sri Lanka on under 5 yr age malnutrition in which prevalence of wasting was 43%[10] A study done by Shela Akbar Hirani in Journal of Ayub Medical College on malnutrition in Pakistani young children shows similar results.[11] Another study on urban slums of Jamnagar city Gujarat India showed prevalence of malnutrition to be 54% among children under five year age.[12]

Maternal nutritional knowledge plays a pivotal and vital role in improving child health that is why various health programmes conducted at different levels aim at improving the maternal knowledge.[13] In this study, out of 195 children, 97(49.7%) had malnutrition. According to determinants of malnutrition amo g the 97 malnourished children illiterate mother 66(68.0%) was the foremost and prime reason followed by residence in rural areas 55(56.7%), low income 52(53.6), toilet absent 28(28.9%) and working mother 24(24.7%).There was a study on children in which the prevalence of malnutrition was noted to be 48.5%. Contributing factors for malnutrition were low income [50.5%], illiterate mother [67.3%], rural area [40.9%], no toilet [35.6%] and working mother [22.6%].[14] The prevalence of malnutrition in another study was noted, it was found to be 54%. Factors linked to malnutrition in this study were low income [73.6%], illiterate mother [54.3%], rural area [59.1%], no toilet [22.5%] and working mother [15.4%].[8]

CONCLUSION

Prevalence level of malnutrition in our children is affrighting, formidable and direful. Mother's education status and living in rural areas villages has a definite association with malnutrition. We should work on improving the knowledge and awareness level of mothers regarding diet of children who are under the age of five years. At each encounter, providers should listen to parental concerns regarding food fads and weaning. Providers can then provide individualized education to address specific concerns or misconceptions. We have to do this with the help of awareness programs in each community, with the help of social media e.g. newspaper, television, publication and lady social workers. Henceforth, our study did not provide an exploratory analysis, but also served as a didactic tool.

Limitations of the Study

The data was obtained from a paediatric unit of a tertiary care hospital. Henceforth, the results cannot be generalized to the population and the sample size is small. The study used a cross-sectional design because of this we were not able to establish causation between the study variables used in our research.

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Conflict of Interest

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Contributions of the Authors

All authors Dr.Sadaf Jabeen, Dr.Sonia Zofishan and Prof.Dr.Ayesha Arif participated in the research conceptualization, data analysis, data interpretation, results, discussion, conclusion and manuscript preparation. Data collection was done by Dr.Sadaf Jabeen and Dr. Sonia Zofishan. All authors have read and approved the final manuscript for submission.

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PROPORTIONS OF ORAL CLEFTS IN PATIENTS VISITING THE CLEFT CENTER OF CHILDREN HOSPITAL & INSTITUTE OF CHILD HEALTH LAHORE

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Abstract

Background: Cleft lip and/or cleft palate (CL/P) are the most common congenital craniofacial anomalies with varying incidence. Etiology of cleft lip and palate is multifactorial

Objective: To update information regarding various types of oro facial clefts in patients visiting orthodontic unit of the dental section of the Children's hospital, Lahore during three year period from 01-01-2016 to 31-12-2019

Methodology: This observational descriptive study included 480 subjects comprising 293 males and 187 females. Age of these patients ranged from one day old to 10 years. The method used for this study was Kernahan modified double 'Y' with numeric coding system. A total of 12 combinations were used to describe all types of clefts. The data was analyzed in SPSS 23 statistical package.

Results: The most common finding of this study was complete bilateral clefts affecting 219 patients (45.62%). The next common type was complete unilateral cleft of the lip and palate occurring in 116 patients (24.16%). Among these, clefts involving left side were more common and were seen in 77 patients (16.04%) compared to 8.12%.complete unilateral clefts of the right side (males 25, females 14). An unusual finding of this study was complete unilateral and partial clefts of the opposite side.

Conclusions: This study concluded that Male were affected more than female in cleft lip and palate cases. The most common cleft type is bilateral complete cleft lip and palate. Left complete unilateral cleft lip and palate is more common in female.

Key Words: Cleft lip, cleft palate, proportions, and incidence

Cleft lip and/or cleft palate (CL/P) are the most common congenital craniofacial anomalies with varying incidence.[1] Boys were more commonly affected by cleft lip and cleft palate whereas girls predominated in the isolated cleft palate cases.

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Epidemiological studies have revealed the incidence to be 1 in 700 around the world with marked geographical and ethnic differences.[2] Asian populations have the highest frequency (1 in 500) with the Caucasian population as intermediate and African population having the lowest (1 in 2500).[3] The reported rate was 1.33/ 1000 live births for Asians, 1.30 for Chinese, 1.34 for Japanese, and 1.47 for other Asians.[4] Incidence of cleft lip and palate in Pakistani population is reported to be 1.91 per 1000 births (one per 523 births).

Etiology of cleft lip and palate is multifactorial. One of the most common factor causing Cleft lip and palate is Hereditary in nature.[5] Other important factors causing cleft deformity includes use of drugs like

corticosteroids and thalidomide, radiations, stress and infections like rubella virus etc.[5]

Cleft lip with or without cleft palate (CL/P) can results from the failure of the fusion of the frontonasal and maxillary prominences during development.[6] Embryological failure of fusion between front nasal process and maxillary process will lead to cleft lip. Cleft of primary palate is caused by the failure of adequate mesodermal migration or proliferation. The cleft of the secondary palate occur because of lack of elevation of the palatal shelves during development.[5]

Many classifications of varying cleft lip and cleft palate deformity have been suggested. Basis of these classifications are morphological and embryological. Embryological classification is devised by Kernahan and Stark.[7] The symbolic 'Y' classification was later on introduced by Kernahan which was further modified into double 'Y' system.[8]

The objective of the study was to update information regarding various types of orofacial clefts in patients visiting orthodontic unit of the dental section of the Children's Hospital, Lahore. This study was aimed to determine the frequency of different types of cleft lip and palate and its geographical distribution in the Pakistani population of Punjab.(Fig 2)

METHODOLOGY

This observational descriptive study was done on patients of cleft lip and/or palate who reported to Children Hospital and Institute of Child Health, Lahore from (01-01-2016 to 31-12-2019). The subjects included in this study were 480 patients (293 male, 187 females), with age ranging from day one to 10 years.

The method applied for this study was Kernahan's Modified Double 'Y' Classification System of Cleft lip and Palate. This classification system was used in this study because it not only provides symbolic illustration with numeric coding system but it can be easily recorded in computer program.(Fig 1)

Clinical examination was performed on chair side to see location of the clefts. After identification, these clefts were related to the numeric codes of symbolic double 'Y' to get Kernahan's classification.

This data was analyzed in SPSS 23 to calculate frequencies and percentages of cleft types and gender cross tabulation. The analysis also included the frequencies and percentages of the areas to which the subjects belonged.

RESULTS

In this study, 293 male patients were examined as compared to 187 females (Table 1). Among the sample, 45.6% patients (males 147, females 72) had complete bilateral cleft of the lip and palate. (Table 1) Complete unilateral clefts were seen in 24.37% patients. Amongst these, clefts involving left side were seen to be more common, affecting 16.04% patients (males 29, females 48) as compared to 8.12%. Complete unilateral clefts of the right side (males 25, females 14).

An unusual type of cleft was examined in 5.98% patients involving unilateral complete and partial cleft of the secondary and soft palate on opposite side. In 2.08% patients (males 6, female 4) complete unilateral clefts of the right side and secondary and soft palate of the left side were observed. Clefts of the secondary and soft palate were identified in 3.54% patients (males 12, females 5). The third largest proportion of clefts examined was the cleft of the median soft palate, found in 7.29% neonates (29 males, 6 female). Further details of findings are given in Table 1.

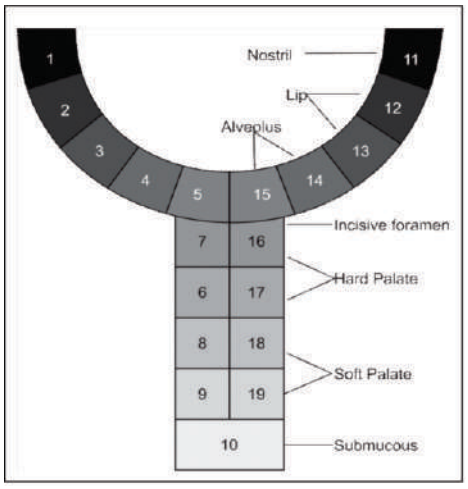

Fig 1: *Kernahan's Modified Double 'Y*

Fig 2: *Geographical Distribution of the Study Population*

Table 1: *Kernahan's Modified Double "Y" Classification Gender Cross Tabulation*

Type of cleft deformity	Sex		Total
	Male	female	
Median Soft palate 8, 9,18, 19, 10	29	6	35
Bilateral Comp cleft lip & palate 1-10-11-19	147	72	219
L complete unilateral 11-19, 10	29	48	77
R complete unilateral 1-10	25	14	39
R cleft nose, lip, alveo- lus, primary palate 1-5	6	6	12
R cleft nose, lip, alveo- lus 1-4	8	3	11
L cleft nose, lip, alveolus 1-15	5	9	14
L cleft anterior to inci- sive foramen 1-5, 15, 14, 13, 12, 11	14	7	21
L alveolus 13,14	3	2	5
Sec & soft palate 6-10, 16-19	12	5	17
Total	293	187	480

The patients referred to the orthodontic unit of the Children's Hospital belonged to different places. Seventeen cities were recorded in the data (Table 2). All patients were referred from both adjacent and remote areas of the Punjab. The highest number of patients presented from the area of the cited hospital i.e., Lahore (n=238, 49.58%). The next larger number analyzed was 49 patients (10.20%) from Kasoor. Only 4 patients (0.83%) presented from Gujrat.

Table 2: *Tabular Representation of the Localities of Cleft Patients*

City	Frequency	Percentage
Lahore	238	49.58
Sahiwal	13	2.70
Gujranwala	9	1.8
Jhang	25	5.20
Sialkot	7	1.45
Bahawalnagar	5	1.0
Sheikhupura	17	3.54
Hafizabad	23	4.79
Ptoki	26	5.41
Multan	10	2.08
Bahawalpur	5	1.04
Narowal	18	3.1
Tobateksingh	10	2.08
Pakpatan	19	3.95
Gujrat	4	.83
Sargodha	6	1.25
Kasoor	49	10.20
Total	480	100

DISCUSSION

In the present study, a larger proportion of male patients were examined; 590 males compared to 370 females. The overall male to female ratio was 1.59:1 in this study which is slightly higher than the study of Aljohar et al[9] who reported it to be 1.3:1. Similar observations were made in a study by Martelli et al[10] with a male to female ratio of 1.7:1 in the cases of a cleft lip and palate. Our results also match with the study conducted by E. Cordero[11] This Contrary to our study, McLeod NM et al[12] reported a male to female ratio of 2.4:1.

Complete bilateral clefts of the lip and palate were found in 53.74% patients comprising the largest pro- portion of the study. This finding was similar to the studies of Blanco-Davila[13] and Bellis et al.[14] In earlier study from our department we mentioned that increased number of clefts patients in our department was due to referral from other hospitals.[5] After the introduction of new methods for nasoalveolar moulding[15] in cleft lip and palate at our center we have atten-

ded the greatest number of bilateral complete cleft patients

Distribution of complete bilateral cleft in our study is 46.04% (146 female and 296 male) which is contradictory to 11% distribution of complete bilateral cleft of the lip and palate comprising 75% male and 25% female patients reported in the literature.[12] Greater occurrence of complete bilateral cleft of the lip and palate in males is however supported by most investigators.

The second most common type of cleft examined in our study was complete unilateral cleft which on the whole were calculated to be 24.37% of all the clefts. Amongst these, clefts involving left side were more common being 16.04% compared to 8.33% clefts involving right side. This result of our study was also supported by Phumzile Hlongwa[16] Increased number of unilateral complete clefts of the left side is supported by most of the reference studies.[11,12]

The third larger proportion examined in this study was cleft of median soft plate. This category comprised of 7.29% patients (60 males, 10 females). The next larger proportion found was cleft involving Left side anterior to incisive foramen. This category comprised 4.5% patients (29 males, 14 females). Some authors[14] have reported the secondary and soft palate clefts as the largest proportion. Their findings are not supported by our current and previously conducted study in our department.[17]

An unusual finding of the current and our earlier[5] study was complete unilateral cleft and opposite secondary and soft palate cleft, examined in 57 infants (7.54%). This type has not been described in the literature in such a detail. This specific finding became possible probably because of Kernahan's modified double stem of the symbolic 'Y' that enabled record keeping of each part and either side of the cleft area. The median line of the double stem of the Kernahan's "Y" represents the mid Sagittal plane. This parameter has enabled the researchers to identify this uncommon type of the cleft.

Statistics on the prevalence of cleft and their clinical outcome are essential for the progress of research, clinical audit and planning of clinical services.[18] Accurate data of congenital anomalies must be maintained by the government agencies to find incidence of oral clefts. Registration of the cleft patients should be made compulsory rather than on voluntary basis, involving government, semigovernment and private sector. In Pakistan no such system has been developed so far. National registry is therefore suggested to develop like other developed countries.[19]

This study can serve as a means of establishing data important for genetic counseling and as a first step in identifying strategies best suited for identification of causes.

CONCLUSION

This study concluded that:

- Male were affected more than female in cleft lip and palate cases.
- The most common cleft type is bilateral complete cleft lip and palate.
- Left complete unilateral cleft lip and palate is more common in female.

Authors' Contributions

Dr. Hamza Nazir designed the initial study, searched related literature, collected data and conducted the study. Dr. Ayesha Ashraf designed the initial draft of manuscript. Dr. Sana Babar worked on literature search, reviewed and finalized results and discussion. Dr. Faizan Ali reviewed the literature, and contributed to the discussion. Dr. Shazia Ramzan and Dr. Nidal Iqbal reviewed the study outcomes and conclusion and made corrections too. All authors contributed to the final manuscript.

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AESTHETIC EVALUATION OF THE NASOLABIAL ANGLE IN THE PAKISTANI POPULATION BY USING CEPHALOMETRIC AND PHOTOGRAPHIC METHOD

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Abstract

Background: The morphological relationship and proportionality between nose, lips and chin determine the facial harmony in orthodontics. Nasolabial angle is diagnostically critical area for an orthodontist as critical examination of this angle appreciates the feeling of proportion and balance with the rest of face.1 Combined cephalometric and photographic analyses provide a thorough diagnostic approach during treatment planning.

Objectives: Assess the aesthetic role and gender difference of nasolabial angle of subjects having orthognathic profile by cephalometric and photographic methods in the selected sample.

Methodology: This Cross-Sectional study included 100 subjects, 50 males and 50 females (15-17years) with class I occlusal relationships were included in the study in department of Orthodontics, The Children' Hospital, Lahore. The data was processed using SPSS 23.

Result: For each variable, mean and standard deviation were calculated. To see any significant difference between the two methods, student's t- test was applied. Each qualitative variable was assessed by frequency and percentage. Chi Squares was used to see the relationship between the attributes. The study revealed that there was no statistically significant difference between the two methods used.

Conclusion: It was concluded that harmony and facial balance are not fixed concepts and variability exist between different populations. During treatment planning gender, age, racial and ethnic differences must be kept in mind for proper measurement and calculation.

Key Words: Aesthetic evaluation, Soft tissue profile, Skeletal class I, Sexual dimorphism, Cephalometric, Facial profile photographs.

Beauty means social power, success, and the combination of qualities such as shape, color, or form that pleases the aesthetic sense especially the sight. Beauty always has a positive influence in all areas of civilized society. Facial beauty is very important in inter human communication. The origin of the human perception of facial beauty dependent on each person's sense of perception and this sensory enjoyment of the observers also depend on their own ideas, feelings and judgments.[1]

Perceptions of facial beauty is multifactorial phenomenon with genetic, environmental, and cultural foundations. The philosopher David Hume said, "Beauty in things exists in the mind which contemplates them" and the writer Margaret Wolfe Hungerford famously said, "Beauty is in the eye of the beholder".[2]

The concept of esthetics is subjective, so it is very hard to determine objective criteria for defining the concept of beauty. However, since the 13th century,

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the mankind has started to notice the common characteristics of beautiful things and named this mysterious attraction the "divine proportion". It was also interpreted as an effect of mathematics on esthetic beauty. The secret of mysterious beauty in Leonardo de Vinci's Mona Lisa might have been an application of the divine proportion to the human face.[3]

Facial aesthetics is one of the main goals of orthodontic treatment planning and uses profile outlines. Orthodontists are now evaluating not only the skeletal structure of face by cephalometric measurements but due to emerging concept of soft tissue paradigm they are also giving due attention to the soft tissue profile.[4]

Hence, a comprehensive soft tissue analysis has been devised in addition to hard tissue cephalometric study. Photographs and lateral cephalograms are being widely used as diagnostic tools for evaluation of soft tissue. This aids in establishing individualized norms for each patient to optimize facial attractiveness.[5]

The angle formed between the base of the nose and upper lip. Two lines are drawn from subnasale, the horizontal line is tangent to the most anterior point of the columella while the vertical line is tangent to the mucocutaneous edge of the upper lip. The Nasolabial angle is one of the angles which show large variation due to ethnicity and genetic predisposition. We get a lot of variation in the measurement of this value. Hence, in literature the mean value of NLA° varies from 80-120 degrees.6

The Nasolabial angle, one of the most important soft tissue angular measurements of nose showed much variation with some authors in the definition and drawing method. Increased angle was found due to a turned up nose or lips that slant back.[7,8]

METHODOLOGY

Hundred subjects, 50 males and 50 females (15-17 years) with class I occlusal relationships were inclu-ded in the study. Lateral cephalograms and profile photographs were taken in standardized conditions. Linear and angular measurements were analyzed for each individual separately on radiographs and photo-graphs. The data was processed using SPSS version 23. For each variable, mean and standard deviation were calculated. To see any significant difference between the two methods, student's t- test was applied. Each qualitative variable was assessed by frequency and percentage. Chi Squares was used to see the rela-tionship between the attributes.

The Cross-sectional study was done. Orthognathic profile with facial convexity angle 160.50° + 4.04. Normal angle case with (SN) and mandibular plane (MP) (SN-MP 32 + 40). After identifying the various soft tissue landmarks, final selection was done on the basis of facial convexity angle and ANB values for the selection of esthetically pleasing profiles.

RESULTS

The study revealed that there was no statistically significant difference between the two methods used. A total of 100 subjects were included in this study, 50 males and 50 females. All had class I dental and skeletal relationships according to our inclusion criteria. The data was analyzed by SPSS 23 and then specific tests for this study were applied. For any test of significance, a p- value of .05 or less was taken to be significant.

The arithmetic mean, standard deviation, minimum and maximum of skeletal characteristics of the sample was calculated using SPSS version 23 as is given in table and the soft tissue characteristic of the sample selected in the photograph was calculated as shown in table which both made the foundation for final sample selection.

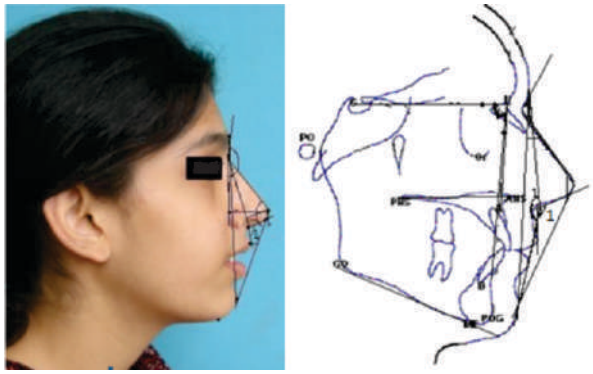

Figure 1: *Photographic Landmarks And Parameters Cephalometric Landmarks And Parameters*

Table 1: Comparison of Angular Measurements Between Males And Females (n= 100) (In degrees)

Sex	Parameters	Mean	SD	S.E.M	t-value	p-value
Male	Nasolabial Angle (cephalogram)	97.79	6.03	.853	1.96	.052
Female		95.66	4.72	.667		
Male	Nasolabial Angle (photograph)	97.88	5.92	.837	1.84	.068
Female		95.92	4.61	.653		

Key: SD : Standard Deviation

For evaluation of sexual dimorphism, Independent t- test was applied and the arithmetic mean, standard deviation, standard error mean, were compared to calculate any significant difference between the two sexes as tabulated in table

According to the table the mean value of cephalometric Nasolabial Angle of males was 97.79°± 6.03°, which is larger than in females who had a mean 95.66°±4.72°. There was no statistically significant difference between males and females in comparison of their cephalometric Nasolabial angle values (p= .052).

There was no statistically significant difference between males and females in comparison of their photographic Nasolabial values (p=.068). The mean photographic Nasolabial values for males was 97.88° ± 5.92°, which is larger than in females who had a mean value of 95.92°± 4.61° indicating that males have larger Nasolabial angles as compared to females.

Table 2: Comparison of Angular Measurements between Cephalometric and photographic methods (n= 100) (In degrees)

Parameters	Mean	SD	S.E. mean	t-value	Df	p-value
NLA1°	96.72	5.49	.549	-.228	198	.820
NLA2°	96.90	5.37	.537			

NLA1 : Cephalometric Nasolabial angle.
NLA 2 : Photographic Nasolabial angle.

Paired t-test was applied to calculate t-value and p-value to measure any significant statistical difference between the two methods of aesthetic evaluation under study. Under standardized conditions, the results obtained were insignificant as shown in table.

Table 3: : Angular Characteristics of Cephalometric and Analogous Facial Photographic Measurements (n= 100) (In degrees)

Parameters	Mean	SD	Min	Max
NLA1°	96.72	5.49	89.00	110.00
NLA2°	96.90	5.37	90.00	109.00

The subjects were computed for the soft tissue parameters of cephalograms and photographs and their arithmetic mean, standard deviation, minimum and maximum values were found and are given in table

NLA1 : Cephalometric Nasolabial angle
NLA 2 : Photographic Nasolabial angle.

DISCUSSION

The visual impact of soft tissue of the face determines the esthetic value of face. In contemporary Orthodontics detailed soft tissue analysis is an important component of comprehensive diagnosis and treatment planning especially after the introduction of soft tissue paradigm. The objective of this study was to aesthetically evaluate nasolabial angle of face by using cephalometric and photographic methods and to find any sexual dimorphism between the values obtained. The present study was carried out on lateral cephalogram and profile photographs of 100 subjects (50 males and 50 females). The angle formed between the base and columella of the nose and upper lip. Two lines are drawn from subnasale, the horizontal line is tangent to the most anterior point of the columella while the vertical line is tangent to the mucocutaneous edge of the upper lip, so measuring angle between columella and line intersecting subnasale and labralesuperius is the most common method practiced by maximum number of respondents to measure nasolabial angle.[9] Nasolabial angle is one of the angles which show large variation due to ethnicity and genetic predisposition. We get a lot of variation in the measurement of this value. The angle can be assessed with the help of photographs, cephalograms or directly on patients however there is a lack of universally accepted method to measure this soft tissue variable.[10,11] Hence, in literature the mean value of NLA° varies

from 80-120 degrees.[6]

The mean value for the cephalometric Nasolabial angle in this study was 96.72° ± 5.49°. The males had marginally larger value of NLA1° (97.79° ± 6.03°) as compared to females (95.66° ± 4.72°).

The mean photographic value for Nasolabial angle was 96.90° ± 5.37°. The males had a mean value of 97.88°±5.92°, which is larger than in females who had a mean NLA2° value of 95.92° ± 4.61°. No statistical significant difference between the two methods for evaluation of Nasolabial angle (p=.820) was found.

These values for Nasolabial angle were quite similar as found by Tajik[12] (102.73° ± 9.75° for males and 95.96° ± 9.61° for females) in normal faces. The values of Nasolabial angle found by Shaikh[13] were similar for males, 100.5° ± 7.5°, but were slightly less in females which were 104° ± 12° in her study. Similarly the values of Nasolabial angle found by Ahmed F[14] in which the mean value for the Nasolabial angle was 100.68°±6.15° that was within the normal range of 102° ± 10°. The males had marginally larger value of NLA (101.16° ± 7.24°) as compared to females (100.20° ± 4.92°).

Zylinski et al[15] compared Nasolabial angle of boys and adult men. The sample comprised of 31 boys aged 5 to 10 years old (mean age = 7.6 years) and 29 men aged 22 to 32 years old (mean age = 26.2 years). Nasolabial angle noted in pre-adolescent boys and adult men were 111.5° ± 7.8° and 110.8° ± 7.6° respectively. He concluded that Nasolabial angle of an individual remains constant. But, his means are larger than what this study reveals.

Fitzgerald et al[16] suggested that measurement of this angle alone provides inadequate information as it does not reveal which component is responsible for the variability. It could be the nose, the lip, or both. Therefore it is important to analyze each component of this angle to assist in the differential diagnosis of normal from its variation. Fitzgerald et al[16] evaluated a comparatively larger sample of 104 young white adults determined by the authors to have well-balanced faces. Nasolabial angle was 114° ± 10°. No statistically significant difference was demonstrated between the values for men and women in this study, but the women had a slightly larger Nasolabial angle. This value is larger than our mean value for Nasolabial angle suggesting ethnic variability.

Hwang H S6 found a NLA of 93.45°+ 8.49° by anatomic point method and 62.25° + 9.99° with the tangent line method. The value given by him by either method was less than our mean value.

Hashim and AlBarakati[17] compared Nasolabial angle of 30 adult Saudi males (96.2° ± 11.1°) to the male sample of Zylinski[15] and noted statistically significant differences (p =0.000) between Caucasian and Saudi sample, which is actually quite close to our mean value of Nasolabial angle, suggesting that Caucasians with balanced profile have slightly obtuse Nasolabial angle as compared to Asian community.

Fernández-Riveiro[18], in her study on adult European Caucasian population (212 individual, 50 males and 162 females, 18–20 years of age), found wide individual variations in Nasolabial angle. In her sample this angle showed large variability, males = 105 ± 13 degrees (range 78.6–131.7 degrees), females = 107.6 ± 8.5 degrees (range 90.5–124.5 degrees). Both of these mean values are larger than our results suggesting acuter Nasolabial angle for balanced faces in Pakistani sample.

Burstone[19] reported the Nasolabial angle of 74 ± 8 degrees (range 60–90 degrees) in a Caucasian adolescent sample with a normal facial appearance. This is less than our values.

Yuen and Hiranaka[20] in a study of southern Chinese population on standardized photographic records reported an angle of 102.7 ± 11 degrees for males and 101.6 ± 11 degrees for females. This value is closer to our results for Pakistani Sample.

McNamara et al[21] reported similar results in a study on lateral cephalograms of adult Caucasians with pleasing facial aesthetics (males = 102.2 ± 8 degrees, females = 102.4 ± 8 degrees), these are again quite similar to our values.

Arnett[22] in his facial planning used photographs of white Americans suggested a mean Nasolabial angle of 106.4° + 7.7° for males and 103.50° + 6.80° for females. American population has more obtuse Nasolabial angle than this study for Pakistani sample suggests.

Scavone H[23] in his photographic study on 60 adult Japanese-Brazilians with normal occlusions and balanced faces found distinct ethnic differences between Japanese-Brazilians and White Americans for soft tissue profile features. He found that despite more lip protrusion in this group, Nasolabial angles were more obtuse due to a more superiorly inclined nose base. His study presented a mean Nasolabial angle of 108.40° + 10.76° for males and 110.10° + 8.7° for females. This shows that Japanese population has more obtuse Nasolabial angle than our Pakistani population, further strengthening the belief that ethnical background determines various facial features and a value which is normal for one race may be unacceptable for another one.

CONCLUSION

Angular measurements i.e. Nasolabial angle showed wide individual variations. It was concluded that Harmony and facial balance are not fixed concepts. During treatment planning sex, age, racial and ethnic differences must be kept in mind.

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KNOWLEDGE ABOUT TUBERCULOSIS AND ITS TREATMENT AMONG NEW PULMONARY TB PATIENTS IN DOTS IMPLEMENTED TERTIARY CARE SETTING AT LAHORE

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Abstract

Background: Pulmonary tuberculosis (PTB) is one of the most serious public health problem and account for majority of all tuberculosis cases. Mycobacterium spread mostly through cases of pulmonary tuberculosis. National Tuberculosis Control Program adopted strategy for identification of cases of TB in which cases are identified passively. Therefore, it is utmost important that the knowledge about TB and services provided under the program is clear in community.

Methodology: A cross sectional observational study was conducted among 180 PTB patient taking treatment of TB from DOTS implemented tertiary care setting of Lahore.

Results: 136(75.6%) of the respondents were aware of TB as a disease. 138(76.7%) patient were aware about one person to other person mode of transmission of tuberculosis. 82(45.6%) were aware about the infective organism as cause of disease. However 129(71.7%) of patients knew about BCG immunization as means of prevention for tuberculosis. Most of the respondents 172(95.6%) believed that tuberculosis is curable.

Conclusion: The current study revealed that although awareness regarding certain basic aspect of tuberculosis was adequate; however there is a great need to improve awareness regarding certain aspects of TB prevention through continuation and innovations in IEC. Availability of free diagnostic and treatment facilities by TB program needs to be appreciated in community.

Key Words: Tuberculosis, Pulmonary tuberculosis, Directly observed therapy short course, Provincial TB control program, Bacillus Calmette Guerin, Information Education Communication.

Tuberculosis (TB) remains a serious cause of illness and death worldwide. There were 9 million incident cases and two million deaths due to TB globally[1]. Pakistan ranks fifth in the 22 high burden countries worldwide.[1] Pakistan declared TB as national emergency in 1994 and adopted DOTS in 1995 to control this major public health problem[2].

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National Tuberculosis Control Program adopted strategy DOTS depends on the patients who present themselves to health care facilities (passive case finding). Poor knowledge of TB symptoms and lack of assess to TB care facilities are important factors for low TB case notification.[3] Therefore, it is utmost important that the knowledge about TB disease and services provided under the program is clear in community.[4]

This study was under taken to assess knowledge regarding symptoms, mode of transmission and awareness about availability of free treatment facilities for TB.

METHODOLOGY

This cross sectional study was conducted at chest

clinic, DOTS implemented center of teaching hospital. The study was conducted among all the 180 PTB patients (study subjects) aged 15 – 55 years currently under treatment for TB. Patients were interviewed at the center. Each interview was conducted at a time when patient was diagnosed and registered in DOTS center. A questionnaire containing socio-demographic variable such as age, sex, religion, literacy status, and knowledge about symptoms, mode of transmission, etiology, prevention and treatment of tuberculosis was prepared as study tool and tested. The collected data was entered in Microsoft Excel and transformed to SPSS statistical package for suitable statistical analysis and inferences were drawn.

Table 1: *Socio- Demographic Profile of Tuberculosis Case n-180*

Socio-Demographic Profile	Number of Cases
Gender	
Male	99(55.0%)
Female	81(45.0%)
Age	
15-54 years	153(85.0%)
55 years and above	27(15.0%)
Marital status	
Married	97(53.88%)
Never married	83(46.11%)
Residential background	
Urban	146(81.11%)
Rural	34(18.88%)
Educational status	
Illiterate	52(28.88%)
Literate	128(71.11%)

RESULTS

A total of 180 TB patients were enrolled in this study. Of these 99(55.0 %) were male and 81(45.0%) female. 146(81.11%) were residing in urban area, 97 (53.88%) were married and 83(46.11%) never married. With regard to the educational status majority of patients 128(71.11%) were able to read and write while 52(28.88%) were illiterate.

Knowledge and awareness about TB disease in the studied population are presented in table-2.It revealed that 136(75.6%) of the subjects have heard of

Table 2: *Knowledge and awareness about Tuberculosis n-180*

Heard about tuberculosis	
Yes	136(75.6%)
No	44(24.4%)
Cause of tuberculosis	
Germs	82(45.6%)
Hereditary	52(28.9%)
Hard work	05(2.8%)
Jodo-Taweez	01(0.6%)
Mental worries	39(21.7%)
Do not know	01(0.6%)
TB transmissible disease	
Yes	138(76.7%)
No	18(10.0%)
Do not know	24(13.3%)
Mode of transmission	
Through droplets	76(42.2%)
Sharing food	56(31.1%)
Smoking	13(7.2%)
Do not know	35(19.4%)
TB is curable	
Yes	172(95.6%)
No	0(0.0%)
Do not know	8(4.4%)
Part of body affected	
Lungs	56 (31.11%)
Other than lungs	0 (0.0%)
Do not know	124(68.88%)
Symptoms of TB	
Cough > than 2 weeks	40(22.2%)
Blood with sputum	97(53.9%)
Do not know	43(23.9%)
TB patient be isolated	
Yes	96(53.3%)
No	68(37.8%)
Do not know	16(8.9%)
Utensils of TB patient be separated	
Yes	103(57.2%)
No	59(32.8%)
Do not know	18(10.0%)
Vaccine against TB	
Yes	129(71.7%)
No	11(6.1%)
Do not know	40(22.2%)
Awareness about availability of current free TB drugs facilities	
Yes	38(21.11%)
No	39(21.66%)
Do not know	101(56.11%)

TB disease before diagnosis of their disease. With regard to the cause of TB 82(45.6%) respondents think germs as a cause of disease; followed by mental worries 39(21.7%). However, 53(29.4%) had no idea about the cause of TB.

138(76.7%) subjects know that it is transmissible disease and 76(42.2%) thought the mode of spread through droplets followed by sharing food 56(31.1%). The majority of respondents172(95.6%) believe that TB is curable disease.56(31.11%) patients know that lungs are mainly affected by this disease. However, 124(68.88%) do not know which part of the body is mainly affected by this disease.

Most of the participants 113(62.8%) believe that TB is not hereditary disease followed by 52(28.9%) those believe that it runs in families. When participants were asked about the symptoms, 43(23.9%) were ignorant of symptoms, 40(22.2%) were of opinion that cough more than two weeks is symptom of TB and 97(53.9%) think blood with sputum as its major symptoms..

With regard to the preventive measures, 96(53.3 %) believe that TB patients should be isolated and 103(57.2%) were of opinion that eating utensils should be separated. However 68(37.8%) and 59(32.8 %) were of opinion that patients should not be isolated and utensil separated respectively. Most of respondent 59(32.8%) know about the BCG.

Only 38(21.11%) of respondent know the current free services for the diagnosis and treatment of TB. With regard to the duration of TB treatment 12(6.7%) replied that duration is 3 months, 33(18.3%) 6 months, and 105(58.3%) told 9 month duration. Only 30(16.7%) participant knew the consequences of incomplete treatment and 117(65.0%) believe that there is no harm in quitting treatment when symptoms are relieved.

DISCUSSION

Level of awareness is considered the most important factor affecting earlier diagnosis, treatment and prevention of TB.

This study showed that majority (75.6%) of patients had heard of TB disease before they were diagnosed as TB patient. The similar findings were observed in previous study where 89.3% of study subjects have heard of TB5. However in one study conducted in Pakistan 27.6% of study subject have never heard about TB before diagnosis[6].

Interestingly, most of the patients think that hereditary, hard work, jado-taweez and mental worries were the causes of TB. Only 45.6% of the patients answered that bacteria/germs were the cause of TB. Our findings are not consistent with other study which has investigated knowledge of TB patients where only 6.9% knew that it is caused by germs[7].

56.1% of the patients answered that lungs are the only organ affected by TB. Similar results were obtained in study conducted in Quetta, Pakistan where (40.0%) of patients think that TB affects lungs only[8]. 76.7% of the patients were of opinion that it is transmittable disease but only 42.2% replied that it spreads through coughing and sneezing. Similar results were obtained in other study conducted in China, 81.20% patients were of opinion that TB is communicable and 61.20% knew that it spread through coughing and sneezing[9]. Correct knowledge among patients about mode of transmission of disease is very important for TB control in their families.

Most of our patients (53.9%) thought that most common pulmonary tuberculosis (PTB) symptom was blood in the sputum and less than 22.2% knew that cough > 2 weeks duration is a symptom of PTB, in other study conducted in West Bengal India, 17% of the patients responded blood in sputum and 21% cough more than two weeks are the symptoms of TB[10]. Poor knowledge about TB symptoms leads to delay in seeking TB diagnosis.

Majority of our patient (95.6%) knew that TB is curable, similar to study conducted in Yamen, where 82.2% patients knew that TB can be cured with the treatment[11]. The knowledge of patients that TB can be cured with treatment can be very helpful in completing full course as prescribed by health care provider.

In our study 76.6% knew that duration of treatment is more than six months. Only 18.3% of our study

know exactly that in DOTS duration of treatment has been reduced to six months. Similar findings (84.5%) were seen in other study[12]. Knowledge of patients about duration of treatment is important as patients knowing this fact are less likely to default and take full course of treatment.

Most of our patients had no idea about the consequences of incomplete treatment. Only 16.7 % knew that TB bacteria can develop resistance against TB medicines. Similar results were obtained in other study in which only 7.3% patient responded that incomplete treatment leads to drug resistant TB[13]. Due to poor knowledge regarding consequences of incomplete treatment, many patients do not take full course of treatment. Poor treatment compliance of TB patients is threat to the emergence of drug resistant TB. Rigorous health education by health worker at the time of registration for treatment may improve treatment outcome and overall TB control

DOTS coverage is 100% in province Punjab and free diagnostic and treatment facilities are being provided by the TB program, however, majority (77.77 %) did not know about this kind of arrangements by the government. This is in contrast to other study finding conducted in India in which 73.5% patients knew that treatment of TB is available free of cost from government health care facilities[14]. Most of study subjects are not aware about availability of free treatment facilities in the city by the government in spite of provincial TB control program efforts. This unawareness can be the cause of under reporting of TB cases. Provincial TB control program should make extensive efforts to disseminate information regarding free treatment of TB by the program.

A majority (57.2%) of TB patient feel that utensil should be kept separate for preventing the spread of disease in contrast to other study where 28.9 % are of opinion that separating dishes can help in preventing Tb[15]. In our study 71.7% of patients knew about TB vaccination in contrast to other study where one third (30.7%) had knowledge about Vaccination[16]. TB patient should be isolated (53.3%). These findings are not consistent with findings of other study done in India where 15.3% responded that isolating TB patient is important preventive measure[17]. Poor knowledge about prevention of TB can cause effect on incidence of disease.

The awareness of TB disease in patients suffering from TB is not so high in spite that this study was conducted in capital of the province and it is alarming sign. As focus of provincial TB control program is on passive case finding, so high number of missing TB cases in province might be due to low level of awareness about TB. There is need to create awareness about symptoms, cause, treatment and prevention of TB through television and radio. Awareness regarding certain aspects of TB can also be done through innovations in Information, Education and Communication (IEC) material. Our TB control program should also focus to increase awareness about the availability of free treatment.

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RELATIVE FREQUENCY AND HISTOPATHOLOGICAL PATTERNS OF DIFFERENT OVARIAN TUMORS AT A TERTIARY CARE HOSPITAL IN LAHORE

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Abstract

Background. The ovaries are a vital part of the female reproductive system. One of the major problems faced by females is the ovarian tumors

Objective: To find out the relative frequency of different benign and malignant ovarian tumors & their histopathological pattern among women of different age groups in the ovarian biopsy specimens received at the histopathology department, Shaikh Zayed hospital, Lahore.

Methodology: A retrospective study was done at histopathology department, Shaikh Zayed hospital, Lahore. The ovarian biopsies of the female patients presenting in the histopathology department were included in this study. The duration of study was one year (January 2020 to December 2020). These biopsies were routinely processed and slides were made. The slides were stained by standard Hematoxylin & Eosin staining and studied under the microscope. The ovarian tumors were classified as per WHO.

Results: The frequency of benign tumors was 51.8% and that of malignant tumors was 48.2%. The surface epithelial tumors were the most common (64.7%) followed by the germ cell tumors (22%).

Conclusion: The surface epithelial tumors were the most common followed by the germ cell tumors. The ovarian tumors are found in all age groups but the frequency of malignant tumors is more in older age group.

Key Words: Ovarian tumors, histopathology

The ovaries are important organ of reproduction in the females. Histological examination had shown that there are different types of cells in the ovary from which numerous neoplastic and non-neoplastic pathologies can arise.[2] These lesions can be benign or malignant. Even the benign ovarian tumors pose a great challenge when they form huge pelvic or abdominal mass and weigh in greater number. Hence, it is very important to classify these tumors for proper treatment.[1] Most of the ovarian tumors present in 50 to 60 years aged women. But the prognosis is good if present in young age less than 40 years of age.[4] PMRC Pakistan medical research council carried a multicentre study regarding frequency of malignant ovarian tumors and found its incidence to be 3.37% in 1973.[5] It has been stated to be the 6th most common female cancer and fourth leading cause of death in women.[6] The ovarian malignancies constitute a major health problem for females in our settings also.[7] 1 in 558 women have life time risk for ovarian cancer as found by the SEER Surveillance Epidemiology and End Results calculations done in USA. Majority of ovarian tumors are diagnosed in advanced stage. This is because the symptoms in early stage are ambiguous and are ignored by the women.[8] In Asia and Japan, the detection rate of new cases is 2 to 7 6.5/100,000 women per year. The delay in diagnosis is due to vain screening tests.

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The precursor lesions are missed and can be detected only after oophorectomy. Some risk factors include nulliparity and family history. Most of the tumors occur in reproductive age group. Microscopically ovarian tumors show various range of patterns. They can arise from epithelium, sex cord or stroma of ovary[7]. It is important to determine the histological pattern for the purpose of treatment and prognosis.

METHODOLOGY

A retrospective study was done at histopathology department, Shaikh Zayed hospital, Lahore. The ovarian biopsies of the female patients presenting in the histopathology department were included in this study. The duration of study was one year (January 2020 to December 2020). These biopsies were routinely processed and slides were made. The slides were stained by standard Hematoxylin & Eosin staining and studied under the microscope. The ovarian tumors were classified as per WHO.

RESULTS

In our study, the age range of the patients was 26 to 74 years (Table 1). The frequency of surface epithelial tumors was the 62%, germ cell tumors 21%, sex cord stromal tumors 13% and other tumors 4%. (Fig 2). The frequency of benign tumors was 54.1% and that of malignant tumors was 45.9% (Fig 1). In our study, no tumor with borderline malignancy was found. We also found that the malignant tumors arouse most frequently in the older age group. (Table 2).

Table 1: *Frequency of Benign & Malignant Tumors in Various Age Groups*

Age range (years)	Benign tumors	Malignant tumors
25 – 35	16	2
36 – 45	12	6
46 – 55	7	8
56 – 65	6	14
66-75	3	10
	44 (51.8%)	40 (48.2%)

Table 2: *Frequency of different histologic Ovarian Tumor types*

Histopathologic diagnosis	n (%)
Surface epithelial tumors	55 (64.7%)
Germ cell tumors	18 (22%)
Sex cord stromal tumors	8 (9.5%)
Others	3 (3.5%)
Total	**85 (100%)**

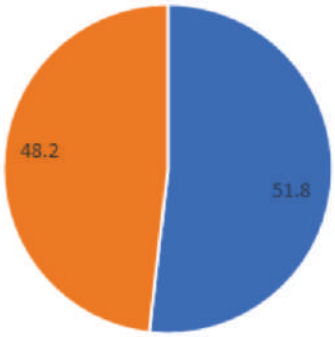

Fig 1. *Frequency of Benign and Malignant Tumors*

DISCUSSION

Our study results are similar to other studies. Like a study done by Iftikhar F et al. showed that most of ovarian tumors were benign and were more common in age group <40 years.[6] The result of our study also coincides with the results of Khan MA et al. They found that ovarian tumors were common between 15 to 29 years and benign tumors were more common than 7 the malignant ones. Yasmin S et al showed in their study that the most common category of ovarian tumors was of epithelial origin followed by the germ cell tumors.[9] Among the benign tumors the commonest benign tumor was serous cystadenoma (24.59%) followed by mature cystic teratoma. In our study, we also found that the most frequent tumors were of serous type. Another study by Thanikasalam revealed that serous cystadenoma was the commonest among Indians and teratomas were the commonest among Malays and Chinese.[10] Prabhakar et al carried out a study revealing similar results. In Belgium, a study by Pilli showed that surface epithelial tumors constituted 70.9% of ovarian tumors being followed by germ cell tumors.[12] This result is also consistent with our study. However, a study by Ong et al found teratoma to be the most common ovarian neoplasm. A study carried out by Hasan Y et al showed 66.41% of ovarian tumors were benign and 24.42% were malignant.[8] In Nepal,

study by R Jha et al reported that 83.9% of ovarian tumors were benign,[13] 16.1% malignant and 2.8% borderline. In Pakistan, a similar study by Ahmed et al showed frequency of benign tumors to be 59.18% and frequency of malignant tumors to be 40.81%.[14] The findings of these studies were consistent with the results of our study.

CONCLUSION

The surface epithelial tumors were the most common followed by the germ cell tumors. The ovarian tumors are found in all age groups but the frequency of malignant tumors is more in older age group.

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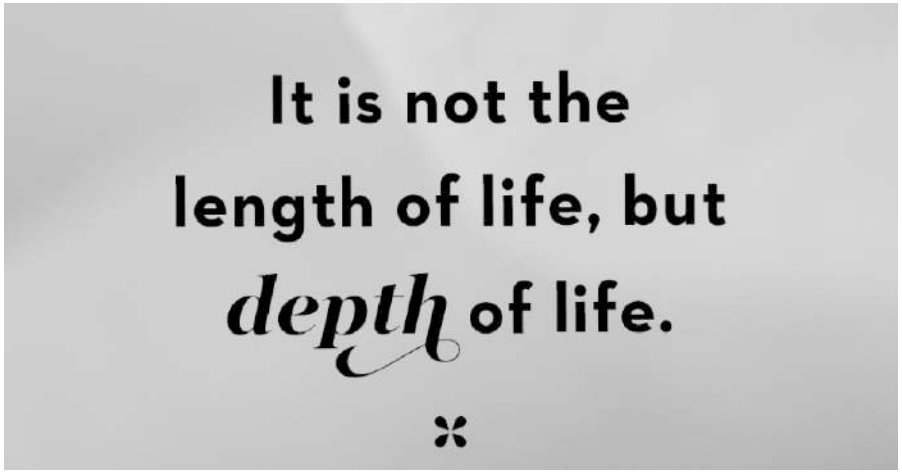

SOCIO-DEMOGRAPHIC STATUS OF NEW SMEAR POSITIVE PULMONARY TUBERCULOSIS CASES REGISTERED IN DOTS IMPLEMENTED TB CARE SETTING

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Abstract

Objectives: Tuberculosis (TB) is a disease of great antiquity and remains a public health problem in Pakistan. TB can infect persons of any age and sex. Age and sex variation in TB prevalence has been reported worldwide. In developed countries people in old age are more commonly infected as compared to developing world where people in younger age are being infected. TB is a social disease with medical aspects. Socioeconomic factors like poor housing, overcrowding conditions, poor quality of life, large families, under nutrition and lack of education have long been associated with TB. After identifying these factors inspired actions can be taken to improve TB control activities.

Methodology: A descriptive observational study was conducted at DOTS implemented TB care facility (Government model chest clinic) of Lahore from January 2019 to December 2019. 316 new smear positive pulmonary tuberculosis cases aged 15 years and above of either sex were selected for the study. Purposive nonprobability sampling technique was used. Cases with previous history of tuberculosis treatment and patient currently receiving anti-tuberculosis treatment were excluded from the study. A detailed history and clinical examination of all selected patients was under taken by the investigator. Socio-demographic data and relevant co-morbid conditions were retrieved by means of a questionnaire. A set of other necessary investigations were also done in all the selected patients. HIV screening was not performed.

Results: A total number of 316 diagnosed cases of new smear positive pulmonary tuberculosis of either sex aged fifteen and above were included in the study. 253(80.06) patients had age range 15-54 years and 63(19.93%) patients were above 55 years of age. 157(49.68%) were male and 159(50.31%) were female. 167(52.84%) patients were illiterate compared to 149(47.15%) patients literate 61(19.30%) patients were smokers. 21(6.64%) patients were using alcohol. BCG scar was present in 94(29.74%) patients. 176(55.69%) patients had body mass index of <20 (underweight). 37(11.70%) patients had family history of tuberculosis. 243(76.89%) patients were living in a room with two or more than two persons. 115(36.39%) patients had family history of tuberculosis.

Conclusion: The socio-demographic presentations of new smear positive pulmonary tuberculosis are heterogeneous. All health care providers, particularly those working with high risk population should have high index of suspicion for tuberculosis, so that diagnosis is not missed.

Key Words: Tuberculosis (TB), Pulmonary Tuberculosis (PTB), Body Mass Index (BMI), Bacillus Calmette-Guerin (BCG)

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Tuberculosis (TB) is a disease of great antiquity and remains a public health problem in Pakistan. The World Health Organization (WHO) estimates that till 2020 the global burden of tuberculosis infection will reach to more than one billion. Surprisingly, more than 80% of the disease burden comes from the poor resource countries where the rate of re-emergence is faster due to poor tuberculosis control and inadequate finances[1]. Pakistan currently ranks fifth amongst countries with highest burden of tuberculosis the

annual incidence of TB being 231/100,000 and about 420,000 new cases are reported annually[2].

It is a social disease with medical aspects. Socio-economic factors like poor housing, overcrowding, poor quality of life, large families, under nutrition and lack of education have long been associated with TB[3]. After identifying these factors stimulated actions to improve TB control activities can be taken. TB can infect persons of any age and sex. Age and sex variation in TB prevalence have been reported worldwide. In developed countries people in old age are more commonly infected as compared to developing world where people in younger age are being infected[4]. Higher rates of tuberculosis have been attributed in people with low socioeconomic status, alcoholics, residents of urban areas and overcrowded situations[5].

The incidence of TB declined in developed countries long before the advent of treatment and vaccination[6]. There is need to take cognizance of socio-demographic factors, so that epidemiological and sociologic approaches can be considered to target tuberculosis control activities in our country. With this in mind, this study was conducted to document the socio-demographic characteristics of new smear positive pulmonary tuberculosis patients who were treated in our department.

METHODOLOGY

A descriptive observational study was conducted at DOTS implemented TB care facility (Government model chest clinic) of Lahore from January 2019 to December 2019. 316 new smear positive pulmonary tuberculosis cases aged 15 years and above of either sex were selected for the study. Purposive nonprobability sampling technique was used. Cases with previous history of tuberculosis treatment and patient currently receiving anti-tuberculosis treatment were excluded from the study.

Informed written consent from subjects was taken before enrolment in the study. A detailed history and clinical examination of all selected patients was under taken by investigator. Socio-demographic data, and relevant co-morbid conditions were retrieved by means of a questionnaire. A set of other necessary investigations were also done in all the selected patients. HIV screening was not performed.

RESULTS

The socio-demographic characteristics of the patients in this study are given in table-1. Among the

Table 1: *Socio-Demographic Profile of Smear-Positive Pulmonary Tuberculosis Cases, n-316*

Socio-Demographic Profile	Smear Positive Cases
Gender	
Male	157(49.68%)
Female	159(50.31%)
Age	
15-54 years	253(80.06)
55 years and above	63(19.93%)
Marital status	
Married	204(64.55%)
Never married	112(35.44%)
Residential background	
Urban	244(77.21%)
Rural	72(22.78%)
Monthly income	
<15,000	298(96.30%)
>15,000	18(3.69%)
Educational status	
Illiterate	167(52.84%)
Literate	149(47.15%)
Occupation	
Housewife / dependent	179(56.64%)
Employed	137(43.35%)
Smoking	
Tobacco used	61(19.30%)
Tobacco not used	255(80.69%)
BCG Scar	
Present	94(29.74%)
Absent	222(70.27%)
Body mass index	
Normal >20	140(44.30%)
Underweight<20	176(55.69%)
Family history of TB present	
No	201(69.93%)
Yes. Reported by family	115(36.39%)
Alcohol	
Alcohol used	21(6.64%)
Alcohol not used	295(93.35%)
Persons per room	
Room sharing present	243(76.89%)
Room sharing not present	73(23.10%)

316 patients with smear positive pulmonary tuberculosis, 157(49.68%) were male and 159(50.31%) were female. 253(80.06) patients had age range 15-54 year and 63(19.93%) patients were above 55 years of age.

In the studied population, 204(64.55%) patients were married as compared to 112(35.44%) patients who never married. 167(52.84%) patients were illiterate, 149(47.15%) patients were literate in educational status. 244(77.21%) patients belonged to the urban areas. Regarding the socio-economic aspect 137(43.35 %) patients were employed, 179(56.64%) patients were house wives/dependents. 298(96.30%) patients had <Rs.15000 monthly income while 18(3.69%) patients were earning >Rs.15000/month. 73(23.10%) patients were not sharing a room with any other person while 243(76.89%) patients were living in a room with two or more than two persons (Table-1).

61(19.30%) patients were smokers. 21(6.64%) patients were using alcohol. BCG scar was present in 94(29.74%) patients. 176(55.69%) patients had body mass index of <20 (underweight).

115(36.39%) patients had family history of tuberculosis (Table- 1).

DISCUSSION

Tuberculosis (TB) remains a major global health problem and is the most frequent cause of death from a single infectious agent. People of all ages can be infected with Mycobacterium tuberculosis bacillus. According to Jae et al (2005)6 and Kaltenbach et al (2001)[7] the presence of pulmonary tuberculosis in elderly patients does not differ much from that in younger patients. Findings of these studies are in contrast to present study where frequency distribution of pulmonary tuberculosis is higher (80.06%) in younger age groups

Holmes et al (1998)[8] reported that the prevalence of infection with Mycobacterium tuberculosis is similar in male and female. Present study also favors the results of the previously conducted study as (50.31 %) of the cases of tuberculosis were found in females in comparison to (49.68%) in males.

It is well documented that pulmonary tuberculosis affects the nutritional status of the patients. A study by Cegielski et al (2004)[9] reported that individuals, with body weight 10% below ideal body weight were three times more likely to become infected with TB. Lonnroth et al (2008)[10] reported that 34% of TB cases were associated with malnutrition. Result of their study corresponds with the present study in which 55.69% of the patient with pulmonary tuberculosis had BMI less than 20.

Tuberculosis is a disease closely associated with poverty. Transmission occurs more frequently in situations where infected persons are in close contact with others in confined spaces. It is well documented that overcrowding increases the risk of disease transmission[11]. This is supported by the present study in which majority of the patients 77% with pulmonary tuberculosis shared rooms.

In the present study 36% of the subjects had history of contact with tuberculosis patient. A study conducted by Pek et al (2002)[12] reported 19% of patients had history of contact with tuberculosis patients. This might be due to living with joint family system in contrast to economically advanced countries. Study from West Africa by Bah et al (2002)[13] reported 33.6% familial TB contact and this is more close to our findings which signifies the association of poverty and room sharing with the development of tuberculosis.

Smoking is considered to be associated with increased risk of infection with Mycobacterium tuberculosis.[14] This is in consistence to the results of present study which showed (19.30%) with pulmonary tuberculosis had history of smoking.

Alcohol use is not independently associated with the development of pulmonary tuberculosis as reported by Moren et al (2009).[15] In the present study only 6.64% had history of alcohol intake.

Regarding the protective effect of BCG in tuberculosis, Hasan et al (2012)[16] reported that 46.4% of previously vaccinated individuals developed PTB. Findings of present study (29.74 % of patient had BCG scar) also supported that BCG played little role in the prevention of the development of tuberculosis.

CONCLUSIONS

In this study, we have reported the socio-demographic profile of new 316 smear-positive pulmonary tuberculosis patients. This study showed that the socio-demographic presentations vary in smear positive pulmonary tuberculosis. All health care providers, particularly those working with high risk population should have high index of suspicion for tuberculosis, so that diagnosis is not missed.

Limitation of study

The main limitation of the present study is relatively small sample size. Secondly this study was conducted in urban area of the province. Further multi centric studies are needed with large sample for identifying factors so that inspired actions can be taken to improve TB control activities.

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Conflict of interest

None

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Contributions of Authors

Aamir Nazir was responsible for the conceptualization and design of the study. Arshad Mahmood Minhas was responsible for data collection, analysis and drafting of the manuscript. Muhammad Hussnain looked after the data analysis and compilation of results. Zamir Ahmad provided guidance in every stage of the study, revised the draft and approved the final version of the manuscript.

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HRCT CHEST IN COVID-19 PATIENTS-DIFFERENT RADIOLOGICAL PATTRENS AND ROLE OF CT INVOLVEMENT SCORE IN PREDICTING PROGNOSIS

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Abstract

Background: HRCT chest is an invaluable modality to study the different radiological patterns and extent of lung parenchymal involvement to quantitate the disease by calculating the involvement score in patients of COVID-19. We can categorize the patients and predict the severity of the disease and its clinical outcome.

Methodology: It was aprospective studyconducted from April 2020 to January 2021.

260 Patients with clinical history of viral chest infection and positive RT- PCR test for COVID 19 were included. HRCT chest were performed on a dedicated multi slice spiral CT scanner. Image interpretation was done according to Radiological Society of North America consensus guidelines. Computerized tomography involvement score was calculated and each CT scan was categorized as mild, moderate and severe disease. These patients were followed for at least two weeks for final clinical outcome.

Results: Our study revealed that on HRCT ground glass opacities were noted in 100% patients. CT involvement score has significant association with final outcome of the patients. Increase in value of involvement score is associated with more critical medical care.

Conclusion: HRCT chest is modality of choice in studying the imaging features of the disease and by calculating the CT-IS we can predict the clinical outcome, when health care facilities are limited and patient load is high. HRCT can be used to categorize these patients and for those with higher CT-IS score intensive care treatment is indispensable.

Key Words: COVID, Real time polymerase chain reaction (RT-PCR), CT Involvement Score (CT IS), Ground Glass Opacities (GGO)

The World Health Organization (WHO) was alerted on 31 December 2019to several patients of a respiratory illness of unknown origin emerging from Wuhan City, Hubei Province of China. The clinical presentations of these patients resemble with viral pneumonia and manifested with fever, cough, myalgia, and dyspnea. These Patients often had pulmonary parenchymal opacities on X-ray chest. In next few months it has affected almost whole world. On 30 January 2020 the World Health Organization declared the disease a pandemic and an emergency of international concern.[1] For early management and to contain the spread of the disease, timely diagnosis plays critical role.

Real time polymerase chain reaction (RT-PCR) test is diagnostic for COVID 19.The specimens are collected from upper respiratory tract of suspected patients.[2,3]

The sensitivity of RT-PCR test on specimens taken from throat is about 30-70%.[4-7] It may be due to faulty technique of sample collection, its transportation

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to laboratories and limitation of testing kits. In the context of COVID 19 epidemic HRCT chest can be a significant alternative to RT-PCR for identification and quantification.[5,6] Imaging with CT chest may be a practical reliable, and quick method to assess the COVID-19.[8] In patients with low viral load when RT-PCR is false negative, HRCT chest shows lung parenchymal changes.[5,6] As the time interval between initial negative and subsequent positive RT-PCR was about 5 days.[5]

However, most of the radiology societies do not recommend HRCT chest as screening test for Covid-19.[9,10] In symptomatic patients CT scan can play vital role in early diagnosis and management.[11] In this study, our aim is to determine the role of HRCT in identifying the imaging patterns and to quantify the disease by CT-IS to define its load and predict the final clinical outcome.

METHODOLOGY

It was a prospective study conducted from April 2020 to January 2021in department of Radiology Jinnah Hospital/ Allama Iqbal Medical Lahore.

Inclusion Criteria: 260-Symptomatic patients of 18 to 80 years having positive RT-PCR for COVID 19 test included in the study. High resolution unenhanced CT chest wasperformed for the detection of viral pneu-monia. Exclusion Criteria: Patients suffering from interstitial pulmonary disease, pulmonary tuberculosis, and malignancy were excluded from the study.

CT chest was done on CT scan machine dedicated only for all COVID-19 suspects. Precautionary measures were taken to avoid cross infection. HRCT chest was among the initial investigations in most of cases as it is readily available with facility of immediate opinion. Patients with signs and symptoms specific for the disease like cough 196, temperature 243, malaise 213, headache 137, sore throat 183, loss of smell 97, diarrhea 72 and difficulty in breathing 130, co-morbidities in 220.Time duration of symptoms and any contact with corona patients were recorded on a questionnaire. Patients were informed about the study and consent was obtained. The maximum time interval between positive PCR test and HRCT chest was 48 hours.

HRCT examinations were performed on dedicated Multi slice helical CT Scanner Philips---Model MX 16 -Slice. Images were obtained from base of neck to mid abdomen in deep inspiratory phase if possible. Slice thickness was 1mm. Images of both lungs were interpreted on lung window (window width 1500 & window level-700) by two senior consultant Radiologists. Multi planer reformatting in coronal, sagittal planes were also performed when required. Findings on HRCT chest were reported as per criteria of Radiological society of North America Consensus Statement.[12] On CT images, presence of ground glass opacitiesin 260 (100%), crazy paving 136 (52.3%), consolidation 193(74.2%), reverse halo sign, architectural distortion 123(47.3%) and pulmonary vessels engorgement in 63 (17.5%) was noted.

The lungs parenchymal involvement was categorized as unilateral in 39 (15%) or bilateral in 221 (85%) with the distribution of the disease in upper lobe in 10(3.8%), middle lobe in 15(5.7%) and lower lobes in 235(90.3%) with predominance of central in 35 (14.0%) patients and peripheral lung zones in 225 (86%). The hazy ill-defined area without obscuring the underlying vessels was defined as ground glass opacity. Crazy paving was defined when it was associated with septal thickening. A homogenous air space opacity obscuring the under lying vessels with & without air bronchogram defined as consolidation. Architectural distortion was associated with fibrosis, sub pleural bands, and volume loss. Dilatation of sub segmental vessels more than 3mm is labeled as vessel engorgement. A ground glass opacity when surrounded by dense crescent shape consolidation was defined as reverse hallow sign.[13] Absence of cavitation, discrete pulmonary nodules, lymphadenopathy and pleural effusion were pertinent negative findings.

The involvement of lungs was calculated on the study model by Chung.[14] All the five lobes of both lungs were evaluated for the degree of ground glass opacity. Score 1 (<5% involvement), Score 2 (5–25% involvement), Score 3(26–49% involvement). Score

4(50–75% involvement), Score 5(>75%). Total CT score was calculated by adding the score of each lobe which ranges from 0 (Normal) to 25 (More than 75% involvement of five lobes.) The disease was categorized as mild (0-9), moderate (10-17) and severe (18-25) on the bases of score range out of total 25. Final clinical outcome of patients was noted after 15 days of follow up as stable without O_2 support, in ICU with O_2 support, on ventilator or expired.

RESULTS

Clinical Analysis. The mean age of the patients was 48 ± 18 with range of 18-80 years. Majority of the patients(65.38%) were between 20 –50 years. Male and female ratio was 1.5: 1.0. with (65.3%) male and (34.6%) females. Fever, cough followed by dyspnea were among initial common symptoms of COVID 19 infection. Most of the patients were having more than one symptom. All the patients with positive RC-PCR test and positive CT chest findings were found symptomatic. 220 (84.6%) patients were having one or more comorbidities. 40(15.6%) patients had no comorbidity. 62 (23.8%) patients had diabetes, 71 (27.3%) patients had hypertension, 23(8.84%) patients in chronic liver disease, 11(4.23%), patients with renal failure and 10(3.84%) patients with malignancy other than lungs, 19(7.3%) patients with heart disease and 24(9.23%) patients with COPD.

CT Analysis. Air space ground glass opacities were noted in 260(100%) of the patients predominantly in lower lobes and peripheral distribution. Other CT findings were crazy paving 136(52.30%), vessels engorgement 123(47.30%), consolidation in 193(74.23 %) patients and architectural distortion/ sub pleural bands 63(24.2%). In this study about (42.30%) patients had CT-IS in mild range (0—9), while(44.6%) with score in moderate range (10—17) and (13.0%) in severe range (18—25). According to CT-IS score total patients in mild category were 110 (42.30%), moderate 116 (44.6%) and severe 34 (13.0%).

Out of 110 Patients having CT-IS in mild range, 30 patients were without comorbidities and 80 patients with one or more comorbidities. 15 patients (13.6%) required hospital admission and received oxygen therapy and I/V medications; all were having co morbidities. But it is significantly less in patients in moderate and severe group. 95 patients (86.4%) received symptomatic treatment and were send for home isolation.

Out of 116 patients in moderate group with CT-IS score (10—17) 10 patients without comorbidities and 106 with one or more comorbidities. 45(38.7%) patients required hospital admission and intensive care life support; 2(1.72%) patients died with co morbidity of un controlled diabetes and chronic decompensated liver disease. 71(61.20%) patients received symptomatic treatment and were kept in quarantine at home or in isolation center.

Out of 34 Patients in severe category (100%) required hospital admission and received intensive medical care with oxygen therapy and I/V medication and ventilator support. 7(20.5%)patients died, all patients had co morbidity 2 with renal failure and 2 with chronic liver disease, 1 with uncontrolled diabetes, 1 receiving chemotherapy for hepatocellular carcinoma and 1 with heart disease. CT-IS score was very well correlated with clinical outcomes including mortality. With increasing CT-IS score, the requirements for critical medical care were also increased. The average time interval between death of the patients and CT scan was 8 days. The patients in mild rage of CT-IS score recovered earlier (mean time 15 days) than the moderate and severe category (mean time 21—28 days).

DISCUSSION

COVID 19 is highly contagious disease, therefore its detection as early-as possible is necessary to prevent its spread and start its early treatment. Patient management and disease containment depends primarily on its early diagnosis.[15-17] In the laboratory testing of COVID 19 is compromised byinherited limitations of kits and by limited resources.[18]

Chest X-ray is less sensitive and specific for the disease therefore leads to false negative results in large number of patients.[19] High resolution CT scan

chest is more sensitive and specific for the detection of opacities in lung parenchyma at an early stage.[20-21]

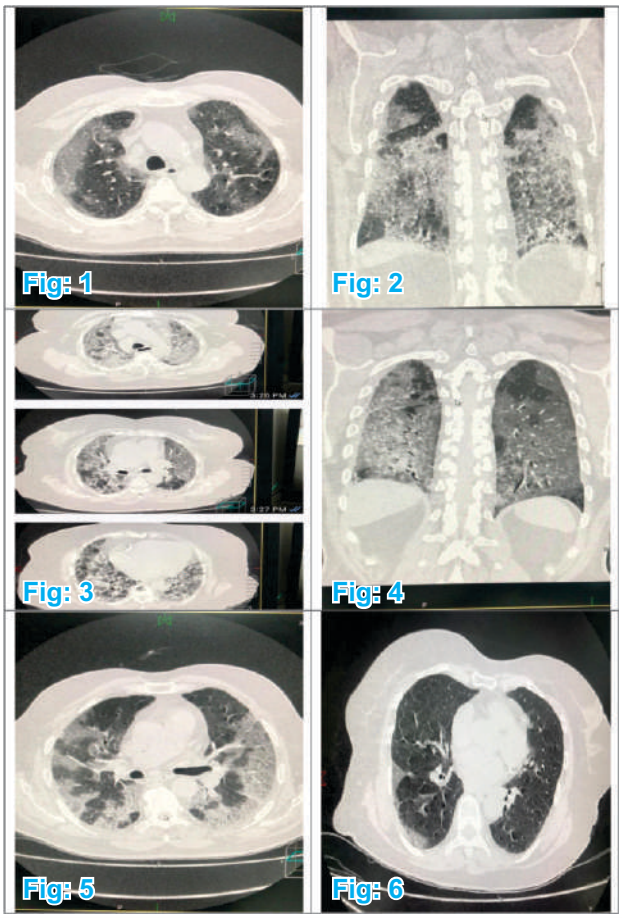
On follow up, high CT-IS positively correlated with increased disease severity and mortality. Patients with comorbid conditions in older age are more prone to contract the disease with more severe sign and symptoms.[22] In Patients of COVID 19 fever was noted in (98%) and cough in (76%).[3]

Review of recent literature shows GGOs (57-100%) and involvement of both lungs in (76—88%) and peripheral distribution in (33—85%).[14,23,26]

Consolidation and crazy paving lung pattern are also reported common findings.[20,22,24,27] Involvement of multiple lobes, particularly the lower lobes are noted in majority of patients in COVID-19 pneumonia.[28] I n our study, results are comparable to recent researches. GGOs were the hall mark findings of our study notedin 100% patients. Consolidation (74.2%) with lower lobe distribution in (90.3%) and peripheral distribution in (86%).

Another important finding observed on CT images was subsegmental enlargement of pulmonary vasculature in 88.7%. Previously this findings was described by Albarello et al and Damiano et al.[26,29] Bai et al also described vascular enlargement in 59 % patients with COVID 19 pneumonia and 22% of patients with non-viral pneumonia.[30] Ye et al suggested that vascular enlargement might be due to pro-inflammatory factors.[31] Other authors also described subpleural bands, Architectural distortion, and reverse halo sign were also noticed in COVID-19 infection.[32] To avoid the variability in reporting the qualitative analysis of our findings categorized as typical, intermediate and atypical based on Radiological society of North America consensus guidelines.[12] Findings on CT Scan for viral pneumonia are general, lacking the specificity for covid-19.[24,33,34]

On imaging it is therefore necessary to distinguish other viral infections from COVID-19 pneumonia which predominantly involves the peripheral parts of lungs but rarely with pleural effusion and lymphadenopathy.[30] In the current pandemic, features of viral pneumonia on CT Chest should be taken as COVID-19 infection unless proved otherwise. The absence of pulmonary cavitation, pleural effusions, and lymphadenopathy noted in our data was also characteristic of previous SARS studies.[8] In our study none of the patient developed pneumothorax. In our study we performed quantitative assessment of CT findings. CT involvement score was done by following the model of Chung et al.[14] Scoring method was based on the opacification of lung parenchyma involving the five lobes of lungs, as a surrogate for COVID-19 burden. We further subdivided the disease as mild, moderate and severe. Patients in severe group of CT-IS, frequently required life sport with increased incidence of mortality. While the patients in mild CT-IS group have better prognosis as compared to patients in moderate CT-IS group. It is important in predicting the medical facilities required for these patients. Another study revealed CT chest - involvement scores have an important role in correlating risk factors in predicting mortality. It may be used as prognostic indicator in



COVID19.[35] In another study extent of CT -IS quantification by visual or using software were predictor of ICU admission or death.[36]

CONCLUSION

On HRCT, chest involvement score is simple method to quantitate the disease. As patients with high CT-involvement score have high mortality rate as compared to patients with low to intermediate CT-IS score. It can be a useful clinical indicator to predict the hospital admission and ICU care especially when we have limited healthcare facilities and patient load is high.

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Limitation of Study PCR Test for COVID was performed at different time interval and from different Labs.

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Conflict of Interest None

Ethical Issue According to the authors there is no ethical issue in this study.

Authors Contributions

Conception & Design Dr. Tanweer Ahmad.

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Final approval of the article Dr. Tanweer Ahmad & Dr. Naeem Ahmad Khan.

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CHARACTERISTICS OF NEWLY DIAGNOSED CHRONIC KIDNEY DISEASE IN PATIENTS WITH DIABETES-A SINGLE CENTER CROSS SECTIONAL STUDY

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Abstract

Objective: To assess the characteristics of new cases of chronic kidney disease in patients with diabetes.

Methodology: The study was conducted in out-patient department of Avicenna Hospital. A study sample of 108 patients was taken who were interviewed on the basis of a well-designedPerforma and all the data were recorded on it. Data was analyzed using SPSS version20 statistical program.

Results: Out of total of 108 patients, 71% (n=77) patients had duration of diabetes more than 5 years. 74% (n=80) patients had history of diabetic retinopathy, 63% (n=69) of peripheral neuropathy, 11.1% (n=12) peripheral vascular disease, while 16.7% (n=18) were having ischemic heart disease.

Among these patients, only 26% (n=28) had good control of diabetes, with HbA1c levels less than 7%. Among lab abnormalities, 94% (n=101) had proteinuria and 39% (n= 42) were found to be anemic. Mean serum creatinine was 2.23 (SD 1.65). Most of the patients were having CKD stage 2, 3 and 4 with percentages of 29.6%, 23.1%, 28.7% respectively. (n=32, 25, 31 respectively).

Conclusion: Majority of the patients were having advance stage of CKD when diagnosed. We suggest physician and patient's education regarding early recognition of the disease so to prevent disease progression.

Key Words: chronic kidney disease, diabetes

Chronic kidney disease (CKD) is considered an important public health problem,[1] as it is associated with increased risk of mortality from any cause, which result in increased in cardiovascular complications and the progression to end-stage renal disease (ESRD) independently of traditional Cardiovascular risk factors.[2-5]

The incidence and prevalence of diabetes mellitus have significantly increased throughout the world, as cases of type 2 diabetes is progressively increasing. This has a major influence on development of diabetic kidney disease (DKD) in diabetic population, which is most common complications observed in type 1 and 2 diabetes patients. DKD is the leading cause of renal failure leading to dialysis, approximately 50% of dialysis dependent CKD cases are due to diabetes in the developed world.[6]

The probability to have a DNP is high in patients with albuminuria and diabetic retinopathy. Absence of diabetic retinopathy in the presence of macroalbuminuria is associated with high chance of non-diabetic renal disease, about 30% of diabetic patients with macro albuminuria without diabetic retinopathy would have non- diabetes associated renal disease. The natural history of DNP is not well established in

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type 2 diabetes mellitus because alterations of glucose metabolism and diagnosis is mostly established many years later. Type 2 diabetes patients are not routinely undergoing renal biopsy, the diagnosis of DNP is made on clinical grounds and nephrologist reserve the option to do renal biopsy in those patients where he suspects non-diabetes associated renal disease or when DNP is questionable. UACR and eGFR assessment annually is recommended as a screening tool for diagnosis DKD in diabetic patients. Early detection of CKD would allow physicians to timely intervene, thus reducing the progression of renal disease as well as associated complication e.g. cardiovascular. The decreased eGFR and/or increased UACR is import predictor to diagnosed CKD in DM2 patients, but it is observed thatsubstantialnumber of DM2 patients maydevelopeddeclinedin eGFR in the absence of increased UACR.[7]

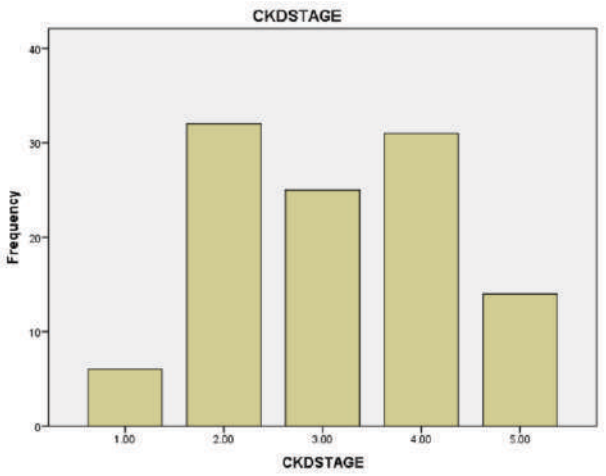
METHODOLOGY

The study was conducted in out-patient department of Avicenna Hospital. A study sample of 108 patients was taken who were interviewed on the basis of a well-designedPerforma and all the data were recorded on it. Data was analyzed using SPSS version20 statistical program.

RESULTS

A total of 108 patients were interviewed with mean age of 55.5 (SD 11.74) among which 50.9% were male (n=55). 71% (n=77) patients had duration of diabetes more than 5 years. 51.9% (n=56) patients were taking insulin, 33% (n=36) were taking oral hypoglycemic while 13 %(n=14) were taking both insulin and oral hypoglycemic drugs. 74% (n=80) patients had history of diabetic retinopathy, 63% (n=69) of peripheral neuropathy, 11.1% (n=12) peripheral vascular disease, while 16.7% (n=18) were having ischemic heart disease.

Among these patients only 26% (n=28) had good control of diabetes, with HbA1c levels less than 7%, while 74% (n= 80) were having bad control of diabetes with HbA1c levels more than 7%. Among lab abnormalities 94% (n=101) had proteinuria. 39% (n= 42) were found to be anemic. 67% (n=69) were having high cholesterol levels. Mean serum creatinine was 2.23 (SD 1.65). Most of the patients were having CKD



stage 2, 3 and 4 with percentages of 29.6%, 23.1%, 28.7% respectively (n=32,25,31respectively).

81.5% n=88 was in follow up with the physician 4.6% (n=5) with nephrologist while 13.9% (n=15) were having no follow up at all.

DISCUSSION

The worldwide burden of Type 2 diabetes mellitus, with its associated complications, is increasing. DNP is most common complication and it is leading cause of ESRD in these patients. The diagnosis is made on clinical assessment and supported by laboratory investigations, the features which support toward diagnosis are persistent proteinuria, progressive or slow declined in eGFR and hypertension. Diabetes and chronic kidney disease (CKD) are major health issue affecting millions of people globally. It is estimated that the prevalence of diabetes mellitus worldwide will be increased to 4.4% in 2030, which mean nearly 366 million people would be diabetic. The population of Middle East, sub-Saharan Africa, and India are region with increased in new cases of diabetes.[1] Another study observed that the number of diabetic patients would increase from 382 million to 592 million people from 2013 to 2035 respectively.[2] According to data from National Health and Nutrition Examination Survey (NHANES), 39% CKD patients are due to diabetes.[4] Billions of dollars from health care budged

were invested on diagnosis and treatment of end-stage renal disease (ESRD) patients in 2013, almost half of it was spend on DKD.[4] This is the reason efforts are made to diagnosed DKD at early stage which may result in improving patient outcomes. In our study we had analyzed the characteristics of newly diagnosed patients of CKD with diabetes mellitus.

Majority of the patients in our study were having stage 2 and 4 kidney disease when investigated for first time. This finding is worrisome and it also signifies that screening is essential in diabetic patients for early detection of kidney disease.

Good diabetes control remains the cornerstone for reducing the cases of DN. DN diagnosis require screening for increased in albuminuria and low eGFR. But these screening modalities have low sensitivity, this shows to find better screening tools, essentially for those diabetic population who are at risk of developing diabetic related complications. Routinely assessment for eGFR is necessary for screening of diabetic nephropathy. Data from NHANES III showed that 30% may have worsening of eGFR in the absence of albuminuria and retinopathy[(2)]. To reduce the incident of CVD, which is leading causeof mortality in Diabetes, depends on optimizing high LDL, cholesterol as well as adequate control of BP. Extra effort is needed to identify potentially reversible risk factors associated with DN to improve patient's outcome. Limitation of our study was, we did not have biopsy proven DN patients in our study.

CONCLUSION

Many of the patients with type 2 diabetes mellitus have never been evaluated for diabetic retino-pathy. Majority of the patients were having advance stage of CKD when diagnosed. Therefore, we suggest physician and patient's education regarding early recognition of the disease so to prevent disease progression.

Authors contribution

Dr. Raheel Pervaiz: Study design and data collection.

Dr. Azhar Waheed: Lead investigator and review of literature, supervised the study draft and final review.

Dr. Azhar Ali: Data collection ,literature review and writing final draft.

Dr. Ayyaz: Statistical analysis of data.

Dr. Amna Umer: Writing references and initial study draft.

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ACCURACY OF PELVIC ULTRASOUND IN DIAGNOSING ADNEXAL TORSION

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Abstract

Background: Adnexal torsion accounts for almost 3% of surgical emergencies. It involves twisting of the ovary and/or fallopian tube leading to either a necrotic ovary or an undamaged ovary with impaired vascularization. The main objective of the study is to analyse the accuracy of pelvic ultrasound in diagnosing adnexal torsion.

Methodology: This descriptive study was conducted in department of Diagnostic Radiology, DHQ Teaching hospital, Sahiwal Medical College, Sahiwalduring1st July 2019 to 31st December 2019.The data was collected from 50 female patients of age range 18 to 45 years. These patients with acute lower abdominal pain clinically suspected for ovarian/adnexal torsion were identified. Relevant information including patient demographics, past medical and surgical history, operative and pathology notes were collected. All retrieved data was then tabulated into an excel sheet.

Results: The average age of patients was 26.3±7.8 years. Of cases with abdominal pain, 43 (86.8 %) were confirmed as cases of ovarian torsion by surgery and matched our inclusion criterion. Out of these 86% cases, patients with other co-existent surgical diagnoses were appendicitis (24.8%), hemorrhagic cyst (22.9%), ectopic pregnancy (21.1%), and others (18.0%). Ultrasound correctly diagnosed 72.1% of ovarian torsion cases and missed 27.9% of these cases (false negatives). Of all diagnosed ovarian torsion cases surgically, 26 (60.5%) were detected on right side and 17 (39.5%) on the left. On ultrasound, out of 31 cases 18 were on right and 13 on left, respectively (p = 0.61).

Conclusion: It is concluded that in case of clinical suspicion of adnexal/ovarian torsion, ovarian sonography is strongly recommended. If volume of ovary is increased simultaneously, examination by using Color Doppler ultrasound is also necessary.

Key Words: Doppler, Diagnostics, Ultrasound, Adnexal, Torsion

Adnexal torsion accounts for almost 3% of surgical emergencies. It involves twisting of the ovary and/or fallopian tube leading to either a necrotic ovary or an undamaged ovary with impaired vascularization. It is common in females in age range of 14 and 45 years.[1] To prevent the loss of ovary or adnexa and associated serious conditions, for example, thrombophlebitis or peritonitis.[2]

Size of an ovarian mass near 5 cm is associated with increased risk factor of ovarian torsion. Diagnosis of an ovarian torsion is challenging because of its vague clinical presentation. Generally, patients with ovarian torsion present with severe lower abdominal pain.[3] Till date, the diagnosis of ovarian torsion has been made on basis of clinical findings.

Adnexal torsion is an exceptional yet noteworthy reason for intense lower abdominal pain and dismalness in females.[4] It is the fifth most common gynecological emergency, with an incidence of 2.7%. Adnexal torsion may include twisting of the ovary, fallopian tube, or

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both. In the event that total ovarian torsion is undiscovered and untreated in time, it can cause serious complications like peritonitis, loss of ovary and may even prove life threatening.[5] Early diagnosis and timely surgical intervention are of utmost importance if adnexal organs are to be preserved and mortality to be avoided .

Since there are no specific signs and symptoms of patient with adnexal torsion, delay in diagnosis is quite common. Findings of Radiological investigations, including gray scale ultrasonography, are also non specific. Colour Doppler sonography has been proposed as an approach to determine the absence of blood flow to a tossed ovary, in this way helping in diagnosis and early treatment of ovarian torsion.[7]

Reports from existing evidence propose that gray scale sonography along with Doppler flow assessment helps in the right analysis of just 66% of clinically suspected cases.[8]

The main objective of the study is to analyse the accuracy of pelvic ultrasound in diagnosing adnexal torsion.

METHODOLOGY

This descriptive study was conducted in department of Diagnostic Radiology, DHQ Teaching hospital, Sahiwal Medical College, Sahiwal during 1st July 2019 to 31st December 2019.The data was collected from 50 female patients of age range 18 to 45 years. These patients with acute lower abdominal pain clinically suspected for ovarian/adnexal torsion were identified. Relevant information including patient demographics, past medical and surgical history, operative and pathology notes were collected. All retrieved data was then tabulated into an excel sheet.

To avoid bias, a second sheet containing only the patients' study number, demographics, and clinical history was sent to a specialized Radiologist for ultrasound of patients at the department of Diagnostic Radiology DHQ Teaching hospital Sahiwal.

The data were analyzed using SPSS version 19.0. All the statistical tests were considered significant at P≤0.05.

RESULTS

The average age of patients was 26.3±7.8 years. Of cases with abdominal pain, 43 (86.8%) were confirmed as cases of ovarian torsion by surgery and matched our inclusion criterion. Out of these 86% cases, patients with other co-existent surgical diagnoses were appendicitis (24.8%), hemorrhagic cyst (22.9%), ectopic pregnancy (21.1%), and others (18.0%). Ultra-

Table 1: *Outcomes of Specificity, Sensitivity, PPV and NPV*

Signs	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
Ovarian edema	0.40 (0.14 - 0.73)	1.00 (0.84 - 1.00)	1.00 (0.40 - 1.00)	0.82 (0.64 - 0.92)
Ovarian enlargement	0.80 (0.44 - 0.96)	0.63 (0.42 - 0.80)	0.44 (0.22 - 0.69)	0.89 (0.65 - 0.98)
Ovarian cyst or mass	0.60 (0.27 - 0.86)	0.59 (0.39 - 0.77)	0.35 (0.15 - 0.61)	0.80 (0.56 - 0.93)
Abnormal ovarian location	0.30 (0.08 - 0.65)	1.00 (0.84 - 1.00)	1.00 (0.40 - 1.00)	0.79 (0.61 - 0.91)
Abnormal ovarian blood flow	0.00 (0.00 - 0.34)	1.00 (0.84 - 1.00)	NA	0.73 (0.56 - 0.86)
Free fluid in the pouch of Douglas	0.20 (0.03 - 0.56)	0.78 (0.57 - 0.91)	0.25 (0.04 - 0.64)	0.72 (0.52 - 0.86)
Presence of fluid around the ovary	0.00 (0.00 - 0.34)	1.00 (0.84 - 1.00)	NA	0.73 (0.56 - 0.86)
Distended fallopian tube	0.00 (0.00 - 0.34)	1.00 (0.84 - 1.00)	NA	0.73 (0.56 - 0.86)
Sites of bleeding within the affected ovary	0.00 (0.00 - 0.34)	1.00 (0.84 - 1.00)	NA	0.73 (0.56 - 0.86)

sound correctly diagnosed 72.1% of ovarian torsion cases and missed 27.9% of these cases (false negatives). Of all diagnosed ovarian torsion cases surgically, 26 (60.5%) were detected on right side and 17 (39.5%) on the left. On ultrasound, out of 31 cases 18 were on rightand 13 on left, respectively (p = 0.61).

Sixteen (37.2%) surgically detected torsions had primary pattern and twenty seven (62.8%) had secondary pattern. On Ultrasound 25(58.13%)were primary torsions and 6 (14.8 %) of secondary torsions, respectively (p=0.48). Finally, among 43 surgically diagnosed torsions, 32 (74.4%) were complete and 11 (25.6%) were partial, on ultrasound 27 (87.5%)cases showed reduced and 4 (12.5 %)showed absent blood flow in ovaries respectively. There was a significant correlation between completeness of ovarian torsion and ovarian blood flow on Doppler examination (p < 0.001).

DISCUSSION

At present, there is no reliable method to confirm the diagnosis of adnexal torsion preoperatively. To prevent the loss of the ovarian function and its potential association with fertility problems, an early diagnosis of an adnexal torsion is needed.[8] Comparing our results with the previous reported findings confirm higher obtained diagnostic value of sonography compared with some studies and lower value compared with others in our survey. In a similar study by Mashiach and colleagues, sonography had diagnostic accuracy of 74.6% for ovarian torsion.[9] However, in a study by Graif et al. a 100% sonographic sensitivity and 93% specificity for space-occupying disease of the ovary were obtained with a positive predictive value of 88% for the diagnosis of ovarian torsion in both in childhood and adolescence.[10-12]

Because of variations in reported diagnostic performance of sonography in diagnosing ovarian torsion, it can be suggested that an ultrasound exam may be used to make a diagnosis in conjunction with clinical parameters; however, this will be most difficult in patients with ovarian torsion because of its nonspecific symptoms and radiological findings.[13-15]

CONCLUSION

It is concluded that in case of clinical suspicion of ovarian torsion, ovarian sonography is strongly recommended. If volume of ovary was increased simultaneously, examination by using color Doppler is also necessary. Considering high specificity of sonography, in cases with increased volume of ovary and lack of blood flow, diagnosis of ovarian torsion is highly likely and the patient should be a candidate for surgical management.

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COMPARISON OF EFFICACY AND COMPLICATIONS OF VATS VERSUS LIMITED THORACOTOMY IN FIBRINO-PURULENT EMPYEMA THORACIC

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Abstract

Background: Empyema thoracic is a disease which is associated with significant morbidity and mortality. The introduction of Video-Assisted Thoracic Surgery (VATS) has offered a safe and effective method for the management of empyema thoracic in its early stage and it is becoming treatment of choice for major thoracic surgeries.

Objective: To compare the efficacy and complications of VATS versus limited thoracotomy {LT} in fibrino-purulent {stage II} Empyema Thoracic.

Methodology: This was a comparative study carried out in Pulmonology and Thoracic Surgery Department, Gulab Devi Chest Hospital Lahore for one year. 100 patients of purulent empyema (PE) were enrolled on the basis of non-probability, purposive sampling. Patients were randomly divided in two groups. Group I was subjected to VATS and Group II to LT. Procedures were done by a single surgical team. Patients were followed for 1, 2, 4 and 8 weeks and were evaluated for complications. All the data was entered SPSS version 20 and analyzed.

Results: There were 43 (43%) male and 57 (57%) female patients. Mean age was 42.45±3.5years in VATS group versus 44.50±4.2years in LT group. Mean hospital stay in VATS group was 7.4±2.4days versus 15.2±3.9days in LT group. Mean pain score was 2.7±0.8 in VATS group versus 4.4±2.3 in LT group.

There was significant difference between both groups for post-operative hospital stay, mean pain score and severity of pain (p-value<0.05). There were more patients in LT group who required blood transfusion as compared to VATS group. Wound infection was present in 2(4%) cases in VATS group and 5(10%) in LT group. There were 3(6%) cases had air leak in VATS group and 7(14%) in LT. The difference in both groups was significant.

Conclusion: It is concluded that VATS is a better management option than LT in fibrino-purulent Empyema Thoracic in terms of lung expansion, control of infection and post-operative complications.

Key Words: Pleural empyema, video assisted thoracic surgery, limited thoracotomy.

Empyema is a suppurative infection of the pleural space.[1,2] Thoracic empyema is one of the general thoracic diseases, and its incidence is increasing worldwide.[3,4] It shows a significant cause of morbidity and prolonged hospitalization.[4] Generally, the most common cause of empyema is pneumonia. Other causes include lung abscess, bronchopleural fistula, esophageal perforation, postsurgical complications, and trauma.[4-7]

A complicated parapneumonic empyema is an effusion for which an invasive procedure is necessary for its resolution, or a parapneumonic effusion on which the bacterial cultures are positive.[8] Empyema can be differentiated into three phases, exudative (Stage I), fibrinopurulent (Stage II), and organizing (Stage III), representing a continuously evolving pro-

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cess that can be arrested by therapeutic intervention.[9]

The acute or exudative stage (Stage I) has been characterized by a thin serous fluid with minimal debris, pH over 7.2, lactate dehydrogenase below 1000 IU/L, glucose over 60 mg/dl, negative culture, and no loculations. The fibrinopurulent stage (Stage II), has been characterized by a thick fluid and thick fibrin strands, pH below 7.2, lactate dehydrogenase over 1000 IU/I, glucose below 60 mg/dl, positive culture or presence of suppuration, and increased loculations in the pleural cavity. The organizing stage (Stage III), in addition to Stage II, is characterized by a thick fibrous peel and scar formation and with a history of symptoms for 3 weeks or more.[2,9-11]

With prompt treatment, the infected pleural space can be effectively treated with tube thoracostomy, fibrinolytics, video assisted thoracoscopic surgery and other less invasive means.[4,12] The initial exudative stage can often be managed either by antibiotic treatment or by surgical placement of a large drainage tube.[4,13] But, is not effective in the fibrinopurulent or organizing stages (Stage II and III), because fibrin in deposits generate a pleural peel and loculation of fluid restricts the expansion of the lung.[4,9,13] Failure of primary treatment or patient delay in seeking health care treatment in Stage I empyema demands surgical intervention, traditionally involving thoracotomy, and decortication.[4]

Video assisted thoracic surgery approach in the treatment of Empyema Thoracic is safe and cost effective procedure.[4,14] Video assisted thoracic surgery is used for many thoracic diseases and it is associated with less post-operative pain, shorter hospital stay, better visualization of thoracic cavity and early return to work.[4,15,16] Many studies show that VATS is successfully used in the management of Fibrinopurulent stage of Empyema Thoracis.[3,4,11,17-19] Due to its limited ability to decorticate lung properly in organizing stage, its role is still controversial in this stage.[19]

The aim of this study was to compare the results of decortication in fibrino-purulent Empyema Thoracis by surgical decortications performed using the VATS and limited thoracotomy procedures. The results were compared in terms of radiologic resolution, functional improvement and post- operative complications.

METHODOLOGY

A comparative study was conducted in Pulmonology and Thoracic Surgery Department, Gulab Devi Chest Hospital Lahore, in one year period from January 2019 to December 2019. One hundred fibrinopurulent empyema thoracis patients were included using purposive sampling technique. Patients aged 14-70 years, of both sexes, who were fit for general anesthesia, with fibrinopurulent empyema thoracis, who failed to respond to aspiration and intravenous antibiotic according to culture and sensitivity, patients who had septations or loculi on ultrasound chest, and patients who had <0.5cm thick pleura on CT chest, were included in the study. Patients who had undergone thoracic surgery previously, with previous posterolateral thoracotomy, fibro-thorax, known malignancy, or who were sputum smear +ve for AFB were excluded from the study. The patients were allocated in two groups randomly by using random number table for true randomization. Each group was comprised of fifty patients. Group I was subjected to VATS debridement/ decortication and Group II to limited thoracotomy. All patients were given antibiotics according to culture and sensitivity but before the report of culture and sensitivity, empirically injection Ceftriaxone 1gm I/V b.i.d was started. The serial x-rays were done to assess the improvement along with clinical assessment and decision for removal of chest drain was made when drained fluid was less than 30ml, sterile on culture and lung has expanded. Patients were followed after 1, 2, 4 and 8 weeks after discharge from hospital and were evaluated for complications i.e. control of infection and lung expansion with the help of clinical examination, spirometry, chest x-ray, chest ultrasound and CT scan chest. Patients were given general anesthesia with single lung ventilation and were positioned in lateral thoracotomy position. An 8cm incision was given on lateral side of chest in the 5th intercostal space. Inter-costal muscles were

approached and dissected along upper boarder of lower rib and chest was operated in 5th intercostal space. Pleural cavity was approached, pus was evacuated, and debridement/decortication was done. Cavity was washed with normal saline, air leak and hemostasis were secured. Two chest drains of 32-F were inserted through separate holes and attached with suction chamber. Chest was closed in layers and antiseptic dressing was done. After giving general anesthesia with single lung ventilation, patients were positioned in lateral thora-cotomy position. Two small incisions of about 1cm were given in the 4th and 6th intercostal spaces at mid axillary line. One port was used for camera, second for suction/manipulation. All the pus was drained, adhesion was broken and debridement/decortication was done. Cavity was washed with 0.9% saline. Air leak and hemostasis was secured with the help of electrocoagulation and sutures. Two chest drains of 32F were put in the pleural cavity through the already present ports, attached with suction chamber and fixed with chest wall with the help of silk sutures. Chest was closed in layers and antiseptic dressing was done. Good post-op care is imperative for early recovery. This includes proper fluid replacement and correction of blood loss. Antibiotics are continued, strong anal-gesics were given, and care of intercostal chest tube drain (ICTD) was ensured. In the post-op evening x-ray chest was done to confirm the correct positioning of ICTD and expansion of lung. Intermittent milking and negative suction were applied to the ICTD to ensure its patency and drainage of fluid. When the drain was nil and chest x-ray showed good lung expan-sion ICTD was removed. Quantitative data was presented with mean± SD. Qualitative data was presented as frequency and per-centage. Chi-square and independent sample t-test was used for statistical analysis. P-value <0.05 was considered as significant.

RESULTS

Preoperative demographic and clinical characteristics of all patients are summarized in Table 1. The study recruited 100 patients (43 men and 57 women) with the mean age of 43.48±3.85 years. Of these, 50 had undergone decortication with the VATS approach, and the remaining 50 had the limited thoracotomy approach. The mean age of patients in VATS group was 42.45±3.5 years while the mean age of patients in LT group was 44.50±4.2 years. Cough was the most common symptom, presented in all patients, followed by fever and chest pain.

All patients had complete lung expansion post-operatively on chest x-rays and CT chest, and no residual fluid was seen in any of the patients post operatively on USG Chest. The mean hospital stay of all the patients was 11.3±3.2 days. There was significant difference between both groups and VATS have shorter hospital stay as compared to LT (p-value <0.05).

In 72 cases mild pain was observed, out of which 38 (76%) belonged to VATS group while 34 (68%) belonged to LT group. In 19 cases moderate pain was observed, out of which 8 (16%) belonged to VATS group while 11(22%) belonged to LT group. In 9 cases severe pain was observed, out of which 4 (8%) belonged to VATS group while 5 (10%) belonged to LT group. There was insignificant difference between both groups (p-value>0.05).

The mean FEV1 after 8 weeks of surgery was 87.4±11.2 with VATS and 79.5±11.6 with LT. The difference was significant (p-value = 0.001). The mean FVC after 8 weeks of surgery was 88.4±15.2 with VATS and 80.2±12.3 with LT. The difference was significant (p-value = 0.004).

There was significant difference between both groups for loss of blood. There were more patients in LT group who required blood transfusion as compared to VATS group. Wound infection was present in 3(6%) cases in VATS group and in 7 (14%) cases in LT group. Difference was insignificant. There were 2 cases in VATS group who had air leak while in LT group there were 11 cases. The difference between both groups was significant.

During surgery 17 patients turned into Postero-

Table 1: *Preoperative Demographic and Clinical Characteristics*

Characteristics					
Age (years)		43.48±3.85			
		Number (n)	Percentage (%)		
Gender	Male	43	43		
	Female	57	57		
Presenting symptoms	Cough	100	100		
	Fever	90	90		
	Chest pain	92	92		
	Breathlessness	52	52		
	Hemoptysis	15	15		
Clinical investigations	Normal BP	70	70		
	Normal JVP	100	100		
	High pulse rate	80	80		
	High temperature	80	80		
	Pallor	73	73		
	High respiratory rate	30	30		
	Lymphadenopathy	10	10		
Lab investigations	Raised ESR	83	83		
	Low Hb (<10gm/dl)	73	73		
	Raised TLC	65	65		
	Raised Neutrophil	65	65		
	Deranged BSL	18	18		
	Normal LFTs	100	100		
	Normal RFTs	100	100		
	Normal Urine profile	100	100		
Radiological Investigations	Chest X-Ray (Pleural Effusion)	100	100		
	USG chest (Thick fluid with debris)	100	100		
	CT chest (Thin rim of pleura containing pus)	100	100		
Spirometry	FEV1	VATS	⩾80	23	46
			50-79	27	54
		LT	⩾80	26	52
			50-79	24	48
	FVC	VATS	⩾80	21	42
			50-79	29	58
		LT	⩾80	24	48
			50-79	26	52

Continuous data presented as mean±standard deviation; BP: Blood Pressure; JVP: jugular venous pulse; ESR: Erythrocyte Sedimentation Rate; Hb: Hemoglobin; TLC: Total Leukocyte Count; BSL: Blood Sugar Level; LFTs: Liver Function Tests; RFTs: Renal Function Tests; USG: Ultrasonography; CT: Computed tomography; FEV_1: forced expiratory volume in one second; FVC: forced vital capacity; LT: Limited thoracotomy; VATS: Video-Assisted Thoracic surgery.

Table 2: *Postoperative Results*

Results*		VATS n (%)	LT n (%)	p Value
Lung Expansion	Chest X-Ray	50 (100)	50 (100)	NA
	CT Chest	50 (100)	50 (100)	NA
Residual Fluid	USG Chest	0 (0)	0 (0)	NA
Hospital stay (days)		7.4 ± 2.4	15.2 ± 3.9	0.000
Severity of pain on visual analogue scale	Mild (< 3)	38 (76%)	34 (68%)	0.807
	Moderate (3-7)	8 (16%)	11 (22%)	
	Severe (8-10)	4 (8%)	5 (10%)	
	Total	50 (100)	50 (100)	
Duration of pain (days)		4.2 ± 1.8	7.3 ± 2.1	0.78
FEV (%)	Baseline	63.2±12.2	61.9±15.3	0.001
	1st week	69.1±10.4	66.5±12.6	
	2nd week	79.6±12.4	71.8±15.4	
	4th week	82.5±13.8	74.6±11.7	
	8th week	87.4±11.2	79.5±11.6	
FVC	Baseline	59.3±15.7	60.5±13.5	0.004
	1st week	67.7±10.4	63.5±14.6	
	2nd week	78.6±14.5	69.2±14.4	
	4th week	85.2±11.6	75.6±14.7	
	8th week	88.4±15.2	80.2±12.3	
Post-op Complications				
Loss of blood	0	10 (20)	0 (0)	0.000
	1 (500 ml)	25 (50)	15 (30)	
	2 (1000 ml)	15 (30)	35 (70)	
Wound infection within hospital stay		2 (4)	5 (10)	0.239
Air leak within hospital stay		3 (6)	7 (14)	0.182
Re-accumulation of fluid		1 (2)	1 (2)	1.000
Conversion into Posterolateral Thorocotomy		5 (10)	12 (24)	0.062

* Continuous data presented as mean±standard deviation; USG: Ultrasonography; CT: Computed tomography; FEV_1: forced expiratory volume in one second; FVC: forced vital capacity; LT: Limited thoracotomy; VATS: Video-Assisted Thoracic surgery.

lateral Thorocotomy. Among these 17 patients 5 were in VATS and 12 were in LT group. So, 17 more patients were included in the study to complete the sample size.

DISCUSSION

Empyema thoracis is a major cause of morbidity and mortality even in this modern age. In the beginning Empyema thoracic can be treated with antibiotics and drainage but if it progresses into fibrinopurulent or organizing stage then simple drainage and antibiotic therapy is not sufficient and a surgical decortication is required.[12] The aim of surgical treatment for fibrinopurulent and organized phases of empyema thoracis is to control infection and evacuate all pus and debris and allow lung expansion by removal of pleural peel from the lung surface.[20] VATS has previously been demonstrated to allow effective drainage of empyemas in the fibrinopurulent stage, although its role in the organizing phase empyema remains controversial.[20]

This series of thoracic decortications compared results for 100 patients, 50 who underwent VATS and 50 who had LT. The groups were well matched with respect to their baseline characteristics. The mean age of 43.48±3.85years, 17 (17%) patients who were of age 18-20 years, 40 (40%) patients were of age 21-40 years, 35 (35%) were of age 41-59 years and 8 (8%) were of age >60years. The male-to-female ratio was 1:1.3. Risk of developing PE is more in females as compared to males. Empyema has no known sexual predilection.[21] One study reported the mean age of patients was 47.4±15.4 years.[20]

One study reported the frequency of cough in 44% cases, chest pain in 52%, breathlessness 40% and constitutional symptoms in 61% patients. These frequencies are far less than that of the present study but not less to be ignored.[20] Ghaffar et al., reported that on presentation productive cough was the most common complain (87%).[22] Misthos et al in their study reported fever as the most common presenting symptom (88%) followed by cough (73%).[23]

In this study all 100% patients had complete lung expansion post operatively on chest x-rays and CT chest, and no residual fluid was seen in any of the patients post operatively on USG Chest. In the present study, the mean hospital stay of patients in VATS group was 7.4±2.4days while in LT group, there was significantly higher mean hospital stay of patients 15.2±3.9 days. Petrakis reported the significant lower mean hospital stay with VATS as 4.5days as compared to LT, i.e. 7.5days.[17]. Mackinlay et al., previously also reported in a randomized controlled trail that mean hospital stay with VATS is significantly lower as compared to LT.[24] Chan et al., also reported insignificant difference for Post-op hospital stay (days) i.e. 21±14.2days with LT and 16± 6.5days with VATS but with VATS also mean hospital stay was high as compared to other studies.[20] Lawrence et al examined 44 patients who presented with empyema thoracis. Thirty of the 42 eligible patients were treated successfully with VATS techniques; the remaining twelve patients needed open thoracotomy for definitive treatment of their empyema. Duration of stay in their open group is significantly longer than in the VATS group (10.3 vs 5.3 days).

In this study, 33 cases in whom no pain was observed, out of which 21 (42%) belonged to VATS group and 12 (24%) belonged to LT group. In 39 cases mild pain was observed, out of which 17(34%) belonged to VATS group while 22 (44%) belonged to LT group. In 19 cases moderate pain was observed, out of which 8 (16%) belonged to VATS group while 11(22%) belonged to LT group. In 9 cases severe pain was observed, out of which 4(8%) belonged to VATS group while 5(10%) belonged to LT group. There was insignificant difference between both groups (p-value>0.05). Chan et al., also reported significant difference between both groups for post-operative mean pain score and calculated the mean pain score in VATS group was 3.9±2.3 while in LT group was 5.3±2.0.[20]

In clinical assessment VATS was much better than Limited Thoracotomy (LT). There was significant difference in hospital stay. The mean hospital stay in LT was 33.72 days both preoperatively and postoperatively but in VATS group this hospital stay was only

18.3 days(p-Value<0.001). This difference was due to the fact of early acceptance of less invasive surgery by the patients and referring physician. Procedure time is equal and requires a fewer intensive unit admission with shorter stay and patients return to work earlier.[24]

Our study reported that, after 8weeks of surgery the mean FEV1 and VC and was significantly greater with VATS [87.4±11.2, 88.4±15.2] than LT [79.5± 11.6, 80.2±12.3]. The difference was significant (p-value=0.001). There was significant difference between both groups for FEV1 and VC results showed that there is better improvement in FEV1 and VC with VATS as compared to LT. One study reported that with VATS, the mean postoperative VC and mean FEV1 was 84.8%±14.9% and 88.6%±19.2% respectively.[25]

When complication rates were compared, it was noticed that there was significant difference between both groups for blood transfusion required to correct anemia because of blood loss. There were more patients in LT group who required blood transfusion as compared to VATS group. Wound infection was present in 3(6%) cases in VATS group and in 7(14%) cases in LT group. Difference was insignificant. There were 2 cases in VATS group who had air leak while in LT group there were 11 cases. The difference between both groups was significant. Literature has also reported that complication rate with VATS was 45.5% while with LT, it was 63.6%. This study also reported that total duration for tube placement, hospital stay, and overall duration of hospital stay was significantly higher in LT group as compared to VATS while mean operative time was insignificantly higher in LT group (although it was higher).[24]

Mackinlay et al. reported a 10% conversion rate from VATS to open thoracotomy[(24)] that approximates the data reported in the current study (10% in the present study). Striffeler et al attribute their 28% conversion rate from VATS to an open procedure in the treatment of fibrinopurulent empyema to advanced stage disease.[25]

CONCLUSION

It is concluded that VATS is a better management option than LT in fibrino-purulent Empyema Thoracic in terms of lung expansion, control of infection and post-operative complications.

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INTRA-ARTICULAR INJECTION OF SODIUM HYALURONATE IN OSTEOARTHRITIS OF KNEE JOINT

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Abstract

Background: Osteoarthritis is a chronic, progressive and degenerative disorder of articular cartilage resulting from imbalance between wear and tear of articular cartilage in every joint.

Objective: To determine the clinical significance of Hyaluronic acid in the treatment of osteoarthritis of knee joint.

To assess the trial level factors which influence the overall treatment effects of hyaluronic acid on pain relief.

Methodology: After IRB (institutional review board approval and written informed consent from the patients this prospective study was carried out in Orthopedics department at Services Hospital, Lahore from Nov 2017 to Nov 2018. Sixty patients visiting OPD with age from 35 to 60 years having clinical and radiological evidence of primary osteoarthritis of Grade-II and Grade-III (Kellgren Lawrence classification) were included We used Visual analogue scale to assess the pain before and after 6 month follow up. We used the WOMAC score for assessment of disability.

Results: The mean age was 56.5 years (38-60 years). There were 40 males (66.66%) and 20 females (33.33%). Radiologically 42 patients had grade II while rest of 18 patients had grade III osteoarthritis. Two patients lost to follow up. There was significant difference in VAS score before 76± 10 and after 48.3 ± 7.4 the treatment at 6 month visit P-value < 0.001

Conclusion: Significant improvement in WOMAC pain subscale was observed at the end of 06 months and compared to the baseline WOMAC pain subscale (from 10 to 4.7) p = 0.0003. WOMAC stiffness subscale had significant difference from baseline and at the 06 month (p = 0.0003). Similarly the physical function improved after six months (p =0.0025)

Key Words: Hyaluronic acid, osteoarthritis, knee joint, viscoelasticity

Osteoarthritis is a degenerative disease with progressive disability as a result of loss of articular cartilage with subsequent structural and functional changes in the affected joint. It is most prevalent in old age and in obese population. It is one of the leading causes of disability in elderly population.[7] Radiologically, it is characterized by decrease in joint space, sub-chondral sclerosis and osteophyte formation because of cartilage damage. The underlying predisposing factors for osteoarthritis are mechanical, traumatic, genetic predisposition, inflammatory conditions, previous joint infections, advanced age, obesity, metabolic and endocrine factors, osteoporosis and ligamentous laxity. The incidence of Osteoarthritis is increasing due to aging population and obesity. The involved joints in preference are Knee, Hip, ankle, spine, Metatarso-phalangeal joints and the inter-phalangeal joints. Knee is the most commonly involved joint as it bears most of the body weight. There are also changes in the lubricating properties of synovial fluid leading to significant pain and loss of function. Regarding the treatment of osteoarthritis the patient is guided for the activity modification, pharmacological

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agents[1] and physiotherapy.[2] Most of these are ineffective after certain period of time as they are poorly tolerated by these patients. New treatment modalities involving viscoelastic supplementation with hyaluronic acid is the next treatment option for osteoarthritis of knee joint.[3,4] A number of systemic reviews addressing the intra articular administration of Hylagon have been performed. It is approved by USA Food and Drug Authority. Hyaluronic acid is a molecule found in abundance in knee joint in synovial fluid and in the joint cartilage.[5] Knee joint has harsh biomechanical environment, because it is avascular, aneural and alymphatic, where the synovial fluid lubricates with special rheological properties. Synovial fluid has also got the characteristics to clear the free radicals and regulates the intracellular activates of protein binding. Progression of knee osteoarthritis is related to the loss of fluid lubrication mechanism.[6] This process results from de-polymerization of endogenous hyaluronic acid from high molecular weight to low molecular weight hyaluronic acid with consequences of synovial fluid having much less mechanical and viscoelastic properties. So, the exogenous hyaluronic acid may be used in knee osteoarthritis as intra articular injection to limit the loss of properties of synovial fluid lubrication and to reduce the endogenous depolymerization of natural hyaluronic acid. Exogenous hyaluronic acid also has anti-inflammatory properties through secondary mechanism and reduces the pain. Its chondro-protective effect lasts for many weeks. The other possible mechanism of action is stimulation of in vivo hyaluronic acid synthesis and anti-nociceptive action induced by hyaluronic acid. It also serves as space filler that allows to stays in the joint. Several recent studies approve the use of Visco-supplementation in the management of osteoarthritis.[8]

The pathological process involved in osteoarthritis is decrease in concentration and decrease molecular weight of hyaluronic acid resulting in much diminished viscosity of synovial fluid.[9] This view leads to the concept of viscoelastic supplementation with hyaluronic acid. This concept first came in Italy and Japan in 1987, later on in 1992 in Canada followed by Europe in 1995 and further in 1997 its clinical use was established in USA after approval by FDA. The different hyaluronic acid formulations are available in market but the most commonly used hyaluronic acid is Hyalgon which is naturally occurring product. Its composition is alternating N-acetyl-D-Glucosamine and D-Glucoronic acid reduces forming β (1-4) and β (1-3) bonds having molecular weight of 6500-10900 Kda.

It is because of high molecular weight that makes it more viscoelastic making it to stay for weeks in joints, with consequences of slow resorption of this viscoelastic material. No long term adverse reaction with this viscoelastic supplementation has been reported. In most of the trials of Hyalgon, the adverse reactions are almost 2-3% and there is no systemic reaction reported. Only there is minor localized pain which resolves within 3 days. In few cases there are chances of pseudo gout. It is unclear whether it is because of hyaluronic acid or it is because of injection procedure.[10]

Hyalgon injections are available in 2mL prefilled syringes. Recommended dose is 1 injection per week for 3-5 weeks, which can be repeated after 6 months.[11]

Knee joint can be injected either through lateral or medial approach. In medial approach we inject in flexed knee or it can be injection with the knee extended through the supro-lateral pole of patella. If there is effusion present in knee joint then first the effusion is aspirated and the injection is given.[12]

METHODOLOGY

This prospective single center clinical trial was conducted at Department of Orthopedic surgery, Services Hospital, Lahore to assess the effects of viscoelastic supplementation with hyaluronic acid in terms of pain relief and disability management. A total number of 60 patients with osteoarthritis with grade II and III (according to Kellgreen Lawrence Score/ classification) were included in the study. All the patients were dealt on OPD basis after proper informed consent and permission from the hospital ethical

committee. Each patient underwent stress radiograph of knee joint AP and Lateral views. The grading was done on the basis of clinical and radiological grounds (According to Kellgren Lawrence classification). All the patients with secondary osteoarthritis, with recent intra-articular injections of steroids (in last 3 months), Bronchial asthma patients on prolonged steroid therapy, patients with rheumatoid arthritis, SLE, Polymyositis, mixed connective tissue disorder, gout, Grade IV osteoarthritis, patients with varus and valgus deformity of knee joint and in patients where the corrective osteotomy for the knee joint arthritis was done, were excluded from the study.

All these patients were given intra-articular injection of hyaluronic acid form the medial knee joint or through the Anterolateral knee joint after adopting complete aseptic measures. A total of five intra articular injections of Hylogon with one injection per week were given for five weeks. All sorts of analgesia were stopped 2 weeks before the injection. Patients were prescribed tablet Panadol 1gm, one at morning and one at evening as rescue analgesia.

Follow-up was done at 2nd and 6th months after the injection. At each follow up pain, stiffness and disability were assessed by VAS and WOMAC score. At each visit VAS scale and WOMAC score were compared. Data from VAS scale and WOMAC score was analyzed using t-test and repeated ANOVA measurements. A p value of < 0.05 was considered as significant.

RESULTS

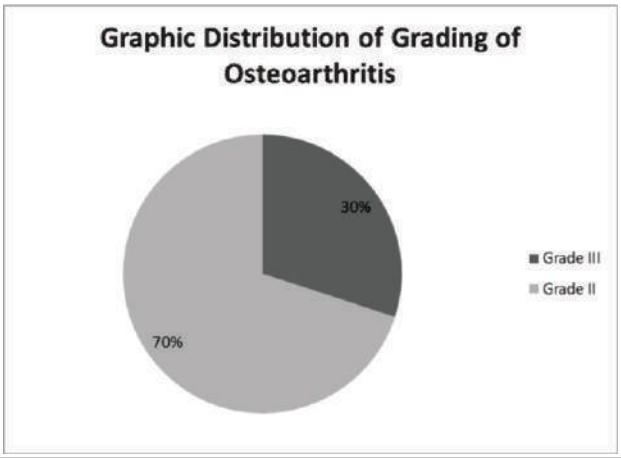
Sixty patients were assessed in the study. The mean age was 56.5 years (38-60 years). There were 40 males (66.66%) and 20 females (33.33%). The symp-toms for the knee pain were present for last 5-7 years in all the patients. Right knee was involved in 45 patients and left knee was involved in 15 patients. Radiologically 42 patients had grade II while rest of 18 patients had grade III osteoarthritis. In our study 60% of our patients were overweight, 10% were obese according to their BMI. Two patients did not come in the follow up. In each patient we used the VAS scale for pain and WOMAC score for assessment of disability at the start of treatment and at second and at 06 months after the intra articular injections of HYALGON. VAS score was 76± 10 before the injections were given and was 77±11 for walking up to 50 meters at the initial assessment. These values dropped to 68.8±8.4 at rest and were 72±10.5 for walking up to 50 meters the end of second month after the last injection which is not statistically significant from the baseline. At the end of 6th month after the last injection, these values improved significantly to 48.3±7.4at rest and 50±6.4 for walking up to 50 meters. ($p<0.0001$).

WOMAC pain subscale was slightly decreased at the end of second month of Intra articular injection of Hyalgon ($p < 0.05$) which was statistically insignificant. Significant improvement in WOMAC pain subscale was observed at the end of 06 months when compared to the baseline WOMAC pain subscale from 10 to 5 ($p = 0.0003$).

WOMAC stiffness subscale had no significant difference from baseline at the second month ($p = 0.812$) while it improved at the 06 month ($p = 0.0003$). Similarly the physical function improved after six months ($p = 0.0025$) form the baseline physical function

Table 1: *Grading of Osteoarthritis according to Gender*

Grading of Osteoarthritis	Male	Female	Total Number of Patients
Grade II Osteoarthritis	30	12	42
Grade III Osteoarthritis	8	10	18
Total	38	22	60



(p<0.005).

No complication was recorded during and at the end of procedure.

DISCUSSION

Osteoarthritis is the major disabling disease of old age1 and represents a significant social burden in a healthcare system. The most important thing is knee pain[3] for which the patient seeks the medical attention. 2nd thing is the clinical and radiological diagnosis of osteoarthritis,[2] as the viscoelastic supplementation is only effective in Grade II to Grade III osteoarthritis. It should be considered in patients with significant symptomatic arthritis who did not respond to NSAIDs and activity modification. It should also be considered in young patients in whom the surgeon wants to delay the total knee replacement in patients who are not candidate for total knee replacement or in whom arthroscopic debridement has failed.[4,5,6] Lot of studies shows the favorable result of hyaluronic acid injection for knee osteoarthritis.[8]

Table 2: WOMAC Subscale Scores for Effectiveness of Intra-Articular Hyaluronic Acid Injection

WOMAC Score per Subscale			p Value Comparison from Baseline
	Mean	SD	
Pain before (baseline)	9	4.5	
Pain after 2 months	9	3	p <0.05
Pain after 6 months	5	2	p <0.0003
Stiffness before (baseline)	4	1	
Stiffness after 2 months	3	1	p = 0.812
Stiffness after 6 months	3	1	p = 0.0003
Physical function before (baseline)	25	7	
Physical function after 2 months	23	6	
Physical function after 6 months	20	4	p =0.0025

Our study comprises of 60 patients having grade II and III osteoarthritis. The baseline VAS score was 76±10 which improved significantly 48.3±7.4 at the end of 06 month after the last injection of hyaluronic acid. The efficacy of intra-articular injection of hyaluronic acid has been established in many clinical trials. It is effective and well tolerated by many patients having grade II and III osteoarthritis of the knee joint.[12] Therefore a larger number of patients experienced pain relief which was sustained till the end of six month. While small numbers of patients still experienced pain similar to the pre-clinical stage. The pain threshold of every patient is different; some patients are able to tolerate pain longer than others.

Our study is also comparable with the study of R.D. Altman et.al.[11] In his study the hyaluronic acid injection reduces the pain and improved the function in osteoarthritis of the knee joint. He used 3-5 injections of hyaluronic acid with weekly interval which were effective in reducing the pain and disability in patients with osteoarthritis of knee joint up to 6 months.

In another study conducted by Leigh Lan et. al. in 2018 also demonstrated the effectiveness of hyaluronic acid for knee osteoarthritis.

The study conducted by Newberry SJ et.al.[14] Also addresses the effectiveness of hyaluronic acid in degenerative osteoarthritis of the knee joint.

In a similar study done by Miller L et.al.[12] Over 8 week treatment with hyaluronic acid, the pain severity decreased to 59% from 55.9±2.8 to 24.4±2.4 (p value of < 0.0001).

In the study conducted by Miltner,[13] "Efficacy of intra-articular injection of hyaluronic acid in patients with osteoarthritis – a prospective clinical trial" has confirmed that 5 intra-articular injections of Hyaluronic acid in osteoarthritis of knee joint provided the pain relief and functional improvement.

All these studies suggest that dealing with the efficacy and safety on intra-articular injection of hyaluronic acid there is increasing evidence that risk benefit balance is favorable to the use of intra-articular injection of hyaluronic acid in knee osteoarthritis.[9] That is why hyaluronic acid injection is recommended for the management of knee osteoarthritis. Moreover it is alternative to unsatisfactory initial pharmacological treatment.[10]

CONCLUSION

It is concluded from study that results of five intra-articular injection of hyaluronic acid given in five consecutive weeks with one injection per week

have significant reduction in pain relief. It also improves the disability and improved the overall functional outcome of the knee joint at least for 6 months.

Ethical Approval

This study was approved by ethical review committee Services Hospital Lahore.

Limitation of the Study

In our study the sample size was small. Moreover the follow up period for the patients under the study was relatively short. There is no comparative arm involved in the study. As long term follow-up would provide more information regarding the functional outcome in patients where the Hyaluronic acid was given in patients with osteoarthritis.

Conflict of Interest None

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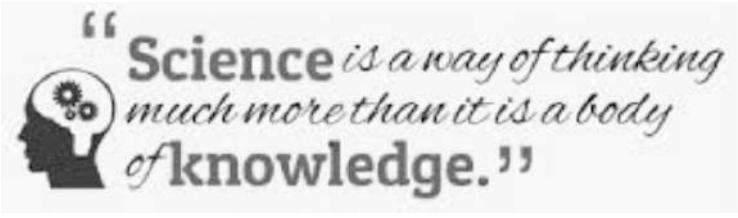

MATERNAL HEALTH ISSUES IN BAGHBANPURA, LAHORE

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Abstract

Background: Health and healthcare provision are essential for the psychological and physical well-being of individuals. Health can most accurately be measured by health outcomes. Our paper aims to assess the maternal health conditions prevalent in Baghbanpura (Shalimar), Lahore.

Objective: To assess maternal health issues in Baghbanpura, Lahore. It ws a community based, cross sectional Study. This study was carried out in Baghbanpura, Lahore. This study was conducted from 1st May 2018 to 30th August 2018.

Methodology: Questions were targeted towards married women to explore reproductive health issues. Respondents were asked about their ideal and actual family size, desired and actual birth intervals, knowledge and usage of contraceptive methods, and the type and kind of ante-natal care received.

Results: Of the 20 households surveyed, 30% of them had more children now than they had initially desired. 75% of the people had heard of contraceptives, but only 30% had used them. 35% of our respondents received no antenatal care at all. Similarly, while 39% delivered their children at home, the rest had different places of deliveries. None faced any serious complications during delivery. During the antenatal period, 70% received dietary supplements such as iron supplements.

Conclusion: It can be concluded that there is a dire need to increase awareness about contraceptive methods in females residing in these areas. 55% of the women in our sample suffered at least one miscarriage. The causes included lack of information about proper antenatal care, physical weakness and mental stress. These healthcare indicators can be improved by increasing the health education through community midwives, religious leaders, electronic and social media.

Key Words: Maternal health, reproductive health, miscarriages, dietary supplements

Health and healthcare provision are essential for the psychological and physical well-being of individuals.[1] The population's health is the major determinant of an economy's productivity. Health can most accurately be measured by health outcomes. Maternal health is the health of women during pregnancy, childbirth and the postpartum period and maternal health care services are antenatal care (ANC), delivery care and postnatal care (PNC) services.[2] Maternal health has been becoming a global concern because the lives of millions of women in reproductive age can be saved through maternal health care services. Despite efforts that have been made to strengthen maternal health care services, maternal mortality is still high in most of the developing countries.[3]

Our paper aims to assess the maternal health conditions prevalent in Baghbanpura (Shalimar), Lahore, therefore, is to improve health outcomes through the improvement of healthcare facilities. Shalimar is one of Lahore's oldest towns and is located on Grand Trunk Road. It is an urban location with a population of low and middle-income households.

The quality of life of a community is highly dependent on the healthcare conditions of the area. Kwon measured the level of health in Korea by looking at structure, process and outcome. Structure refers to the inputs in the system such as medical facilities.

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Process is the activities to improve health outcomes such as calculations of health indicators. Lastly, outcome refers to the objective and subjective indicators of health levels and consumer satisfaction. Objective indicators include mortality and morbidity whereas subjective indicators are based on self-assessment.[4] Most important focus of our work was birth control. A study conducted in 2011 in Karachi shows that although 81% of the sample was aware of the contraceptive methods, 51% did not use any form of contraception.[5] They concluded that although people were aware of birth control techniques, there was a lag in practice,[5] again proven by our research. The objective was to assess maternal health issues in Baghbanpura, Lahore. It was a community based, cross sectional Study. This study was carried out in Baghbanpura, Lahore. This study was conducted from 1st May 2018 to 30th August 2018.

METHODOLOGY

Questions were targeted towards married women to explore into reproductive health issues including ideal and actual family size, desired and actual birth intervals, knowledge and usage of contraceptive methods, and the type and kind of ante-natal care received. A total of 20 households, belonging to different socio-economic backgrounds were interviewed. Res-pondents' ages ranged from 20-60 years while the average age was 36. Respondents had been living in Baghbanpura for an average of 17 years. The average number of people/household was 6.5 and the average number of children of respondents was 3.35.

When asked about health facilities availed inside the locality, 80% people mentioned going to a private clinic/dispensary, 15% to the Government Center and 5% to a hakim. For facilities outside the locality, a different picture emerged as 75% respondents went to a government hospital and 25% to a private hospital. One explanation was the high cost of private hospitals as compared to government hospitals, while the quality was more or less the same.

RESULTS

The average age at which women got married was 18.7 years. The average age at which women had their first child was 20 years. Of the 20 households surveyed, 30% of them had more children now than they had initially desired. Two of the respondents also told us about their wish to have a specific number of children of a specific gender (Table 1).

Table 1: *Fertility Preferences*

House-hold Number	Age at Marriage	Age at First Child Birth	Number of Children Desired	Number of Children Actually Had	Actual Children> Desired Children
1	22	24	2	1	NO
2	17	20	3	3	NO
3	17	29	4	4	NO
4	20	21	3(2 boys, 1 girl)	3(all boys)	NO
5	22	23	2	3	YES
6	23	25	4	3	NO
7	18	20	Many	1	NO
8	18	19-20	4(2 boys, 2 girls)	5(4 girls,1 boy)	YES
9	22	23	3	3	NO
10	18	20	Not aware	5	-
11	22	26	Not aware	4	-
12	16	17	5	4	NO
13	17	18	4	4	NO
14	16	17	Not aware	6	-
15	19	21	2	3	YES
16	8	16	2	2	NO
17	20	21	3	4	YES
18	18	21	1	2	YES
19	20	22	2	4	YES
20	21	22	3	3	NO

1) Contraceptive Awareness and Usage

A look at Table 2, shows that most women had more children than desired due to poor utilization of contraceptives. 75% of the people had heard of contraceptives, but only 30% had used them. In two households, women had used contraceptives while their husbands were unaware of their decision.

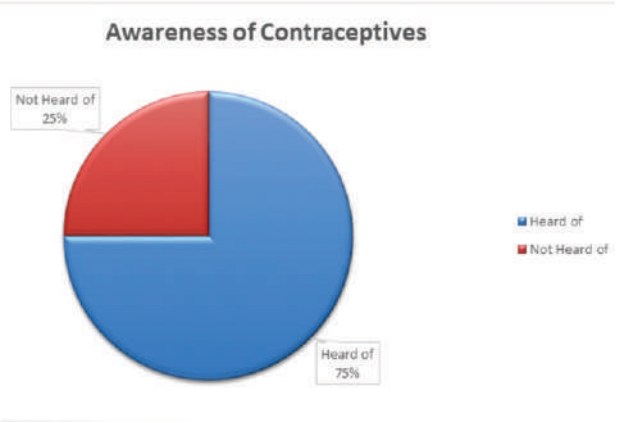

Figure 1: *Awareness of Contraceptives*

Table 2: Contraceptives Usage and Awareness

Household Number	Heard of Contraceptive Methods	Used Contraceptive Methods	Reason If Not Used	Form Used	Joint Decision*
1	YES	NO	Want more kids	NA	NA
2	YES	NO	No need	NA	NA
3	YES	NO	No need	NA	NA
4	YES	YES	NA	IUCD operation	YES
5	YES	YES	NA	Condoms	YES
6	YES	YES	NA	Injections	YES
7	YES	NO	Want more kids	NA	NA
8	NO	NO	Unaware	NA	NA
9	YES	NO	No need	NA	NA
10	NO	NO	Bad for health	NA	NA
11	NO	NO	NA	NA	NA
12	YES	NO	No need	NA	NA
13	YES	NO	No need	NA	NA
14	YES	YES	NA	IUCD operation	NO
15	YES	NO	No need	NA	NA
16	NO	NO	Unaware	NA	NA
17	YES	NO	Want for kids	NA	NA
18	YES	YES	NA	Injections	NO
19	NO	NO	Unaware	NA	NA
20	YES	YES	NA	Condoms	YES

*This means both the husband and wife's decision.
NA: Not Applicable

2) Reproductive Health Issues:

35% of our respondents received no antenatal care at all. The rest had varied choices of health care providers. Similarly, while 39% delivered their children at home, the rest had different places of deliveries (Figure 3). None faced any serious complications during delivery. During the antenatal period, 70% received dietary supplements such as iron supplements. Our respondents severely lacked information about reproductive health issues. 55% of the women in our sample suffered at least one miscarriage. The causes included poor health education, physical weakness and mental stress. There was only one neonatal death, due to the incorrect severing of the umbilical cord. Figure 6 shows the relationship between the miscarriages suffered and the antenatal care received by those mothers. 38% of the miscarriages were suffered by women who had received minimal or no antenatal care. No cases were reported by the women who received antenatal care from the Government Center or Kot Khawaja Saeed Hospital. Surprisingly, 71% of the miscarriages were cases where the mother had taken dietary supplements during pregnancy.

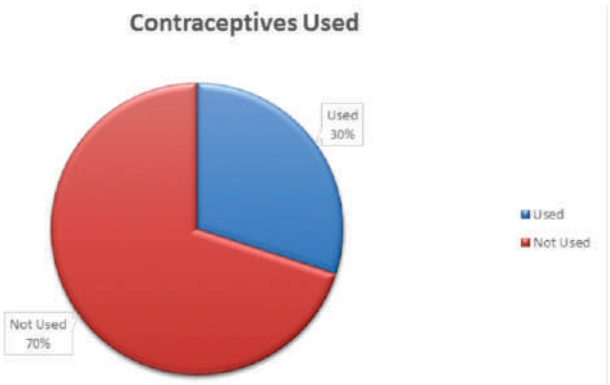

Figure 2: *Contraceptive Usage*

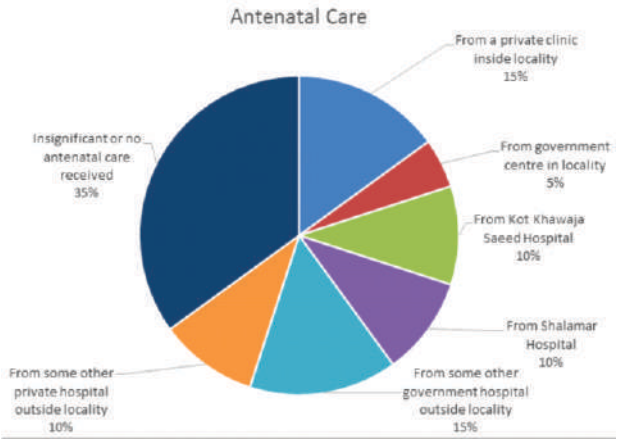

Figure 3: *Antenatal Care Received by Respondents*

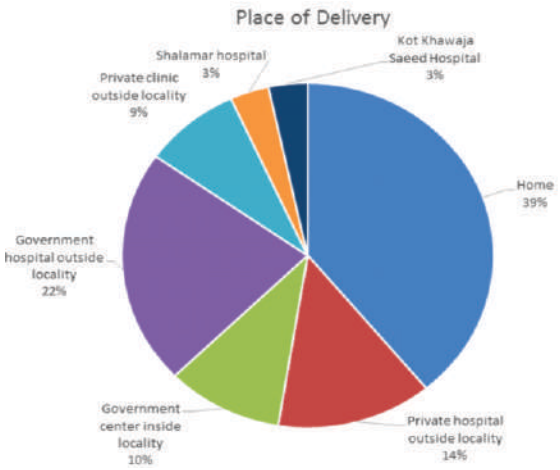

Figure 4: *Place of Delivery of Respondents*

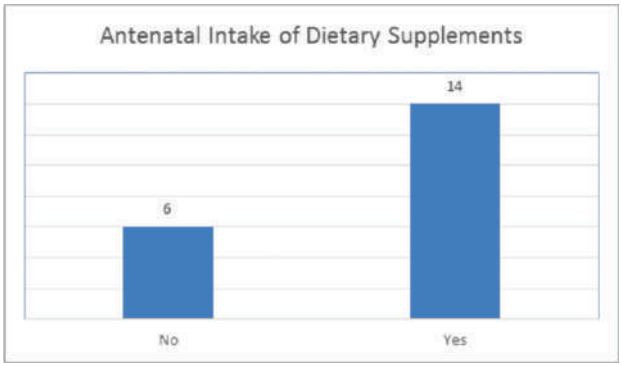

Figure 5: *Antenatal Intake of Dietary Supplements by Respondents*

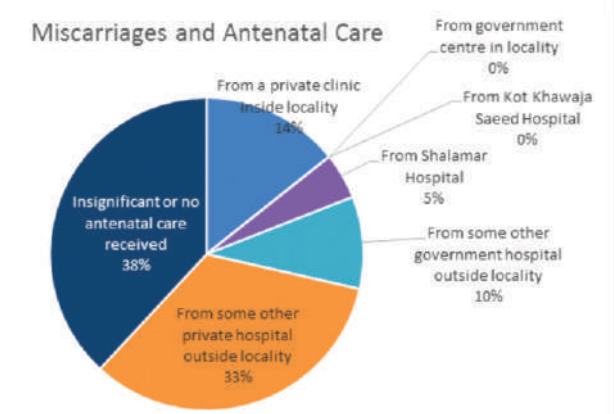

Figure 6: *Miscarriages and Antenatal Care*

DISCUSSION

Contraception is the central pillar of family planning. Modern contraceptive methods and family planning have played a pivotal role in the economic development and progress of various developed nations across the globe. Nonetheless, despite the advent of the modern methods of contraception and their easy availability, population growth has not decreased proportionally in the developing world. 75% of the people had heard of contraceptives, but only 30% had used them. Consistent with our results, a previous study conducted in Pakistan also found that women who accepted family planning services or those who acknowledged the public advertisements of contraceptive methods were more likely users of modern contraceptive methods, unlike those who did not consult family planning services at all.[6,7]

35% of our respondents received no antenatal care at all. Similarly, while 39% delivered their children at home During the antenatal period, 70% received dietary supplements such as iron supplements. A study in India found similar results. ANC use remains in low and middle-income countries for several reasons, including poverty, low educational levels, and lack of access to a health facility.[8]

The maternal mortality ratio (deaths/100,000 live births) given by Kot Khawaja Saeed Hospital for the area was 180, which can be compared to Punjab's figure of 227 and Pakistan's figure of 260. Another study assessed the maternal health care seeking behavior and associated factors of reproductive age women in rural villages of Haramaya district, East Ethiopia and found that regular utilization of maternal health care services reduces maternal morbidity and mortality.[9]

One possible limitation of our research is the relatively small sample size of 20 households, which cannot be seen as completely representative of the area. We could have added more private clinics and hospitals to further strengthen our supply-side analysis. However, since some private clinics opened after 7 pm, they could not have been interviewed due to time constraints. Another limitation was that the research group consisted of three female students and one female supervisor. Due to the cultural sensitivity of the area, some male respondents were unwilling to provide information. Some women were also reluctant to share personal and highly sensitive information.

CONCLUSION

To conclude, there is a dire need to increase awareness about contraceptive methods in females residing in these areas as of the 20 households surveyed, 30% of them had more children now than they had initially desired. 55% of the women in our sample suffered at least one miscarriage. The causes included lack of information about proper antenatal care, physical weakness and mental stress. These healthcare indicators can be improved by increasing the health education through community midwives, religious leaders, electronic and social media.

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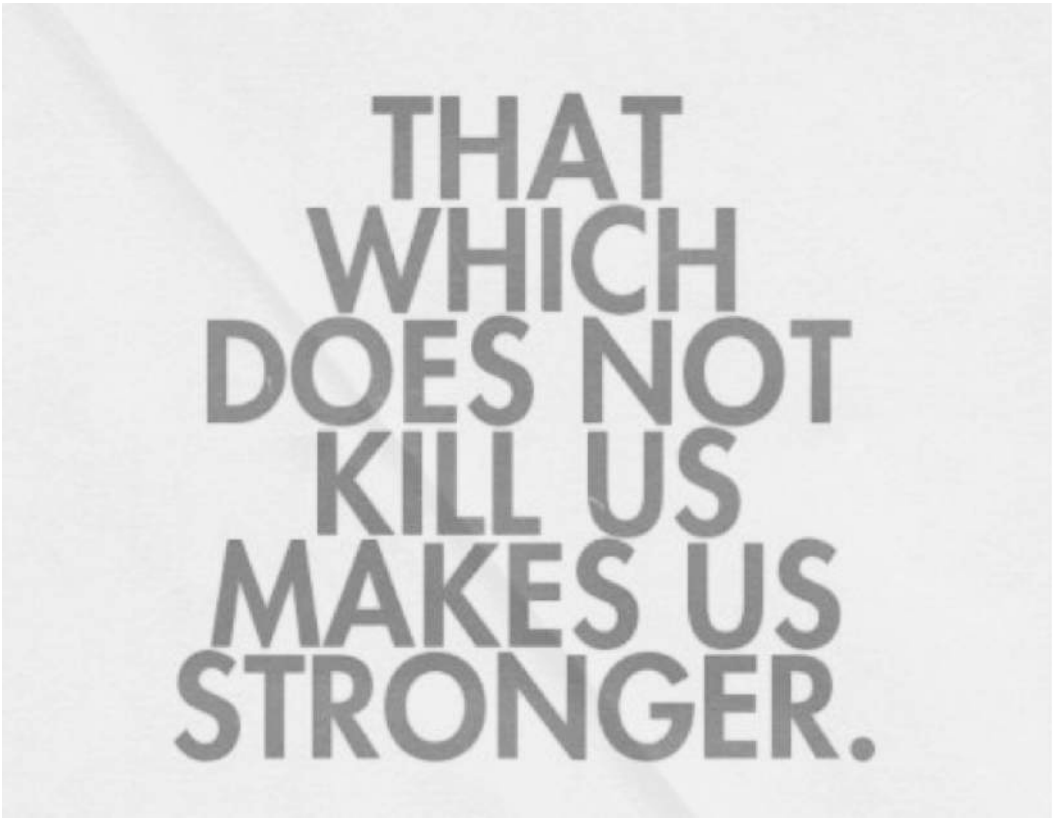

ASSOCIATION OF LOW AMNIOTIC FLUID INDEX WITH ADVERSE FETOMATERNAL OUTCOMES

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Abstract

Background: Oligohydramnios and hence low or borderline AFI is considered associated with raised incidence of complications particularly in high-risk pregnancies. These mainly include meconium aspiration after birth, reduced fetal heart rate, low Apgar score and increased incidence of cesarean section.

Objective: To determine the association of low amniotic fluid index with adverse fetomaternal outcomes. This study was carried out at Gynecology and Obstetrics Department, Jinnah Hospital, Lahore. This study was conducted from 1st June 2019 to 30th November 2019.

Methodology: A total of 302 pregnant women were included in the study. Patients with low amniotic fluid index were included in low amniotic fluid index group or Exposed Group (A). Patients with normal amniotic fluid index were included in normal amniotic fluid index group or Un-Exposed Group (B). All patients were followed up till delivery and adverse fetomaternal outcomes were noted.

Results: Emergency caesarean section was seen in 60 (39.7%) patients in Group A as compared to 30 (19.9%) patients in Group B (p=0.000, R.R = 2). Meconium-stained liquor was seen in 44 (29.1%) patients in Group A as compared to 18 (11.9%) patients in Group B (p=0.000, R.R = 2.4). Birth asphyxia was seen in 6 (4%) patients in Group A as compared to 1 (7%) patient in Group B (p=0.055, R.R = 6). NICU admission was seen in 95 (62.9%) patients in Group A as compared to 42 (27.8%) patients in Group B (p=0.000, R.R = 2.26).

Conclusion: It can be concluded that an amniotic fluid index of ≤ 5 cm detected after 34 completed weeks of gestation is an indicator of poor perinatal outcome.

Key Words: Low amniotic fluid index, Adverse fetomaternal outcomes, Association

Amniotic fluid estimation is very important in pregnancy as increase or decrease in AFI is indicator of some complication in pregnancy. Oligohydramnios can complicate about 1–5% of pregnancies and most commonly it prompts labour induction.[1] One of the most common ways to assess oligohydramnios is to check for Amniotic Fluid Index (AFI). AFI was first ever defined by Phelan in 1987 and it is now a validated tool for accurate estimation of amniotic fluid volume.[2,3]

AFI is estimated by using ultrasound to measure the amount of amniotic fluid volume in 4 quadrants of the abdomens and all are summed up. AFI between 5–8 cm is considered as borderline.[4] Oligohydramnios and hence low or borderline AFI is considered associated with raised incidence of complications particularly in high-risk pregnancies. These mainly include meconium aspiration after birth, reduced fetal heart rate, low Apgar score and increased incidence of cesarean section. (4,5) AFI ≤ 5cm is associated with all these complications during pregnancy; however, borderline AFI has shown different and variable results in many studies. Luo et al conducted a trial and compared the outcome between patients with borderline and normal AFI. They found no significant difference in fetal distress and neonatal mortality between two

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groups. However, the incidence of cesarean rate was significantly higher in patients with borderline AFI.[6] In a study by Bhattacharya R, et al has showed that frequency of emergency cesarean section was 15% in patients with low amniotic fluid index as compared to 9% in women with normal amniotic fluid index, Low Apgar score 11% versus 5% and NICU admission was 65% versus 28%.[7]

However, over the last decades, some authors have found that diminished amniotic fluid index alone is not associated with intrapartum complications, increased caesarean rates or other adverse perinatal outcomes.[8,9,10] As there is no consensus in literature regarding the low AFI, I have planned this study with the objective to determine the association of low amniotic fluid index with adverse fetomaternal outcomes. Result of my study will help to generate further local evidence in this subject. The objective of the study was to determine the association of low amniotic fluid index with adverse fetomaternal outcomes.

Low amniotic fluid index: It was defined as if AFI ≤ 5 cm on ultrasound.

Normal amniotic fluid index: It was defined as if AFI > 5 cm on ultrasound.

Adverse fetomaternal outcomes: It was in terms of following

Emergency Cesarean Section: Emergency cesarean section was defined as any cesarean delivery that was not planned or scheduled and done due to fetal distress.

Fetal Distress: Fetal distress was determined by an abnormal fetal heart rate pattern heart rate (greater than 160 bpm heart rate or less than 120 bpm heart rate) diagnosed by auscultation and continuous electronic fetal monitoring (EFM).

Meconium-stained liquor: It was defined as when amniotic fluid is tinted green or yellow, instead of being clear on visual examination.

Birth asphyxia: If the newborn not breathing (> 90 seconds) or gasping and chest not rising symmetrically with frequency >30/minute on physical examination and an umbilical artery blood test show pH of <7.1 by laboratory test

Low Apgar score: It was defined as Apgar score at 5 minutes after delivery ≤ 5.

NICU admission: It was defined as neonate admission to NICU due to fetal distress.

It was hypothesized that the low amniotic fluid index was associated with adverse fetomaternal outcomes.

METHODOLOGY

Study Design: A Cohort Study.

Setting: This study was carried out at Gynecology and Obstetrics Department, Jinnah Hospital, Lahore.

Duration of Study: This study was conducted from 1st June 2019 to 30th November 2019.

Sample Size: Sample size was calculated with 5% level of significance with power = 80%.

By using expected proportion (birth asphyxia) in population 1 = 4%[8] and expected proportion (birth asphyxia) in population 2 = 0%.[8]

Estimated sample size n = 302

Total sample size was divided into two groups. 151 sample size for low amniotic fluid index group or Exposed Group (A) while 151 sample size for normal amniotic fluid index group or Un-Exposed Group (B).

Sampling technique: Non-probability consecutive sampling

Inclusion Criteria

- Women age: 20-35 years
- Singleton pregnancy on ultrasound
- Gestational age 34-40 weeks on LMP
- Parity 0-4
- Patients with low amniotic fluid index were included in low amniotic fluid index group or Exposed Group (A).
- Patients with normal amniotic fluid index were included in normal amniotic fluid index group or Un-Exposed Group (B).

Exclusion Criteria

- H/o any uterine surgeries on medical record

- Second trimester bleeding on medical record
- Polyhydramnios (AFI> 24 cm on ultrasound)

Three hundred and two patients fulfilling the inclusion criteria from indoor department of Gynecology and Obstetrics Department, Jinnah Hospital, Lahore were included in the study after permission from ethical committee and research department of CPSP. Basic demographics (age, gestational age, parity, AFI level) were noted and Informed consent was taken from each patient, ensuring confidentiality and fact that there was no risk involved to the patient while taking part in this study.

Women were divided in two equal groups. 151 sample size for low amniotic fluid index group or Exposed Group (A) while 151 sample size for normal amniotic fluid index group or Un-Exposed Group (B).

All patients were followed up till delivery and adverse fetomaternal outcomes (emergency cesarean section, meconium stained liquor, birth asphyxia, low Apgar score and NICU admission) as per operational definition were noted and recorded by researcher herself on especially designed proforma. All patients with low AFI were efficiently managed throughout pregnancy as per standard protocol. Data was analyzed with statistical analysis prog-ram (IBM-SPSS 23). Frequency and percentage were computed for qualitative variables like parity, emer-gency cesarean section, meconium-stained liquor, birth asphyxia, low Apgar score and NICU admission. Mean ±SD was presented for quantitative variables like age, gestational age and AFI level. Chi-square test was applied to compare both groups for adverse fetomaternal outcomes taken p ≤0.05 as significant. Relative Risk was also calculated.

Stratification was done with regard to age, gestational age, parity to see the effect of these variables on adverse fetomaternal outcomes. Post stratification using the chi-square test for both groups, p ≤0.05 was considered statistically significant. Relative Risk was also calculated.

RESULTS

Emergency caesarean section was seen in 60 (39.7%) patients in Group A as compared to 30 (19.9%) patients in Group B (p=0.000, R.R = 2) as shown in Table-I. Meconium-stained liquor was seen in 44 (29.1%) patients in Group A as compared to 18 (11.9%) patients in Group B (p=0.000, R.R = 2.4) as shown in Table-II. Birth asphyxia was seen in 6 (4%) patients in Group A as compared to 1 (7%) patient in Group B (p=0.055, R.R = 6) as shown in Table-III. Low Apgar score was seen in 16 (10.6%) patients in Group A as compared to 7 (4.6%) patients in Group B (p=0.050, R.R = 2.29) as shown in Table-IV. NICU admission was seen in 95 (62.9%) patients in Group A as compared to 42 (27.8%) patients in Group B (p=0.000, R.R = 2.26) as shown in Table-V.

DISCUSSION

Assessment of AFV during the antenatal period is considered a helpful tool in determining who is at risk for potentially adverse perinatal outcome.[11]

In the present study, emergency caesarean section was seen in 60 (39.7%) patients in Group A as com-

Table 1: *Comparison of Emergency Caesarean Section in both Groups. n=302*

Emergency Caesarean section		Group A n=151	Group B n=151	P Value R.R
	Yes	60 (39.7%)	30 (19.9%)	0.000
	No	91 (60.3%)	121 (80.1%)	2
	Total	151 (100%)	151 (100%)	

Table 2: *Comparison of Meconium-Stained Liquor in both Groups. n=302*

Meconium stained liquor		Group A n=151	Group B n=151	P Value R.R
	Yes	44 (29.1%)	18 (11.9%)	0.000
	No	107 (70.9%)	133 (88.1%)	2.4
	Total	151 (100%)	151 (100%)	

Table 3: *Comparison of Birth Asphyxia in both Groups. n=302*

Birth asphyxia		Group A n=151	Group B n=151	P Value R.R
	Yes	6 (4%)	1 (7%)	0.055
	No	145 (70.9%)	150 (99.3%)	6
	Total	151 (100%)	151 (100%)	

Table 4: *Comparison of low Apgar Score in Both Groups n=302*

Low Apgar score		Group A n=151	Group B n=151	*P Value* *R.R*
	Yes	16 (10.6%)	7 (4.6%)	0.050
	No	135 (89.4%)	144 (95.4%)	2.29
	Total	151 (100%)	151 (100%)	

Table 5: *Comparison of NICU Admission in Both Groups n=302*

NICU admission		Group A n=151	Group B n=151	*P Value* *R.R*
	Yes	95 (62.9%)	42 (27.8%)	0.000
	No	56 (37.1%)	109 (72.2%)	2.26
	Total	151 (100%)	151 (100%)	

Table 6: *Stratification of Low Apgar Score with Respect to Gestational Age in both Group*

For gestational age 34-36 weeks				
		Low Apgar score		P value
Group		Yes	No	R.R
	A	10(12.3%)	71(87.7%)	0.269
	B	6(7.2%)	77(92.8%)	1.7
For gestational age 37-40 weeks				
Group		Yes	No	
	A	6(8.6%)	64(91.4%)	0.057
	B	1(1.5%)	67(98.5%)	5.8

pared to 30 (19.9%) patients in Group B (p=0.000, R.R = 2). Meconium stained liquor was seen in 44 (29.1%) patients in Group A as compared to 18 (11.9%) patients in Group B (p=0.000, R.R=2.4). Birth asphyxia was seen in 6 (4%) patients in Group A as compared to 1 (7%) patient in Group B (p=0.055, R.R = 6). Low Apgar score was seen in 16 (10.6%) patients in Group A as compared to 7 (4.6%) patients in Group B (p= 0.050, R.R = 2.29). NICU admission was seen in 95 (62.9%) patients in Group A as compared to 42 (27.8%) patients in Group B (p=0.000, R.R = 2.26). This is partially in agreement with that of Ghike et al.,[12] who observed that most of the women in both the groups were either nulliparous or Para one. Conversely, Jagatia et al.,[13] reported that the incidence of oligohydramnios was more in primipara (52.0%) which is compatible with the study of Jandial et al.,[14] and Petrozella et al.,[15] who showed that the incidence of oligohydramnios was 60.0% in primigravida. Such dissimilarities among the results of the above mentioned studies and the present one could be attributed to the differences in the chosen design for the study, sample size and the criteria of its selection.

A possible explanation of the above findings might be related to the fact that oligohydramnios is mostly associated with fetal distress which requires an early interference through induction of labor.[16] Concerning the current study finding of the significantly higher proportion of abnormal fetal heart rate (fetal deceleration) in the oligohydramnios group,[17-19] and[12] asserted that the most strongly associated characteristics with oligohydramnios was the higher percentage of women with abnormal fetal heart rate. Also, in agreement with the present study finding Voxman et al.,[20] and Jandial et al.,[14] observed that, women with oligohydramnios were significantly (p=<0.005) more likely to have abnormal fetal heart rate tracings. This agrees with the current study finding which revealed that 52% of women who complained from oligohydramnios had late decelerations. Moreover, 7.0% of women who had oligohydramnios had fetal beat to beat variability compared to 3.0% of women in the control group. The FHR pattern changes and decelerations can be explained by the poor placental functions associated with oligohydramnios. This results in deficient fetal oxygenation and fetal asphyxia which results in abnormal FHR changes.

Conversely, the rate of CS was higher in oligohydramnios group. This is in coherence with Hanafy[22] who reported that there is statistically significant increase in the rate of C.S in oligohydramnios group compared with those in the control group (40.0% vs. 20.0% respectively).

In addition, Kahkhaie et al.,[23] observed that CS was done in 20.2 % in oligohydramnios group and 8.6% in control group. Also, Ahmad and Munim[27] noticed a more than two fold higher CS rate in the isolated oligohydramnios group (42.0%) compared to 18% in the control group.

Thus, CS was mostly the best option to overcome the adverse effect on the perinatal outcome. Concerning fetal outcomes, the present study showed significantly better Apgar score at the first and fifth minutes among

babies with normal amniotic fluid index than those with oligohydramnios. This is like Chate et al.[24] who noticed that the Apgar score of the study group was less than 7 in 30% at 1st minute, and 16% at 5th minute. Furthermore, Golan et al.,[26] reported a low Apgar score at fifth minutes in 4.6% of neonates. While Ahmad and Munim[27] noticed that the Apgar scores at one and five minutes after birth did not show a significant difference between the two groups (P= 0.575). In this respect, Sarno et al.,[28] noted a significantly higher rate of fetal distress and low Apgar score in women with oligohydramnios. This is reported to be due to head and cord compression.

Meconium staining is an indicator of fetal distress and has its own complication in the newborn. This finding is similar to many research studies; Chandra et al.,[18]; Sriya et al., (81In addition Jandial et al.,[14] observed meconium stained liquor in 48.0% of women with oligohydramnios. While, Youssef et al.,[29] identified it in 40.0% of the oligohydramnios group. This suggests that there is high incidence of meconium staining and poor placental reserve in oligohydramnios group.

CONCLUSION

It can be concluded that an amniotic fluid index of ≤ 5cm detected after 34 completed weeks of gestation is an indicator of poor perinatal outcome. It is recommended that; determination of AFI through regular antenatal care visits can be used as an adjunct to other fetal surveillance methods to identify those infants at risk of poor perinatal outcome.

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FREQUENCY OF MEASLES COMPLICATIONS IN VACCINATED VERSUS UNVACCINATED CHILDREN AND ITS OUTCOME

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Abstract

Background: Measles is a common public health problem around the world and is more prevalent in children below five years of age. It is endemic throughout the world and epidemics tend to occur mostly during spring season. Mostly, it is transmitted through respiratory tract by droplet spray during prodromal period (seven days prior and seven days after rash appearance). It is vaccine preventable viral disease and is likewise a leading source of death in children less than five years of age.

Objective: To find the frequency of vaccination status in children with measles and to compare the frequency of measles complication and its outcome in vaccinated versus unvaccinated children. This Descriptive case series study was conducted at Pediatric Department, The Children Hospital and Institute of child's Health, Lahore during 1st February, 2020 to 31st January, 2021.

Methodology: Total 198 patients with measles were enrolled into the study. Vaccination status was recorded and all these patients were observed about 2 weeks stay in hospital for complications of measles and outcome was assessed in terms of recovery or death. All the findings were recorded and analyzed using SPSS software v25.0. Qualitative variables were compared using Chi-square test. Data were stratified for gender, age and weight. Post-stratification, Chi-square test was applied taking p-value ≤0.05 as statistically significant.

Results: Total 198 children with measles were selected for this study. There were 86(43.4%) males and 112(56.6%) females. Mean age of the children was 8.7±4.31 year. According to outcome distribution, mortality was observed in 5.3% patients with vaccination, while 14.9% patients died with un-vaccination with a p-value 0.023.

Conclusion: The vaccination program in Pakistan for production of immunity against measles, is insufficient and the children who are vaccinated with measles vaccine before their first birthday should be considered unvaccinated and should receive two doses of measles vaccine according to the standard schedule. Vaccination at the age of 12-15 months and a booster dose of measles vaccine at 4-6 year of age can bring the disease under control in the future. Further investigation is needed.

Key Words: Vaccination, Measles complications

Measles is a common public health problem around the world and is more prevalent in children below five years of age. It is endemic throughout the world and epidemics tend to occur mostly during spring season. Mostly, it is transmitted through respiratory tract by droplet spray during prodromal period (seven days prior and seven days after rash appearance).[1] It is vaccinated preventable viral disease and is likewise a leading source of death in children less than five years of age.[2-3]

According to World Health Organization (WHO), before the launch of measles vaccine almost 2.6 million children expire yearly but latterly worldwide this number has decreased to around 71 percent i.e. from 548000 to 158000.[3] In Pakistan, the expected deaths due to measles are 81,000 yearly among children less than five years of age.[4] Major complications of measles leading to mortality in children less than five

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years of age are pneumonia, severe diarrhea, dehydration, ear infections and encephalitis.[5]

Globally, measles remains one of the leading causes of childhood mortality, regardless of the availability of a safe, effective, comparatively inexpensive vaccine. It is also one of the leading risk factor of childhood blindness in the developing world.[6] Additionally around 30% of presented measles cases have one or more complications which are more common among children less than five years of age.[7-8] Vaccination for measles is a live attenuated vaccine which produces mild or non-communicable infections.

Measles antibodies develop in about 95% of children vaccinated at twelve months of age and 98% of children vaccinated at fifteen months of age.[9] Adequate immunization coverage results in significant reduction of incidence, morbidity and mortality from measles.[10] In Pakistan, measles vaccine course is given as a double dose at the age of nine months and fifteen months. The vaccination plan for measles in Pakistan remains below 60%.[11] The main reasons for failure to vaccinate are the lack of information and lack of motivation.[12]

In vaccinated group, complications include bronchopneumonia in 49(49%), upper respiratory tract infection in 39 (39%), diarrhea in 32 (32%), ulcer in 31(31%), dehydration in 15(15%), otitis media in 10(10%), malnutrition in 2 (2%), encephalitis in only 1(1%) case. In non-vaccinated group, bronchopneumonia in 51(51%), diarrhea in 50 (50%), upper respiratory tract infection in 24 (24%), oral ulcer in 22 (22%), dehydration in 20 (20%), otitis media in 17 (17%), malnutrition in 12 (12%), and encephalitis in 11 (11%) patients.[13]

The risk of measles complications and death is higher in non-vaccinated cases and vaccination is defense against the incidence of complications and death.[14] The purpose of this work is to determine the frequency of measles complication and its outcomes in vaccinated and unvaccinated children. There have been studies elsewhere but in our setup no such study has been conducted. The result of this study added to existing body of knowledge. The results may be used by policy makers, planners, managers and practitioners to institute meaningful interventions for the benefits of general populations. The objectives of the study were to find the frequency of vaccination status in children with measles and to compare the frequency of measles complica-tion and its outcome in vaccinated versus unvacci-nated children.

Measles: Prodromes of fever 99.9F, cough, coryza and conjunctivitis, koplik spots, maculopapular rash spreading down from the face to the trunk over 3 days.

Complications

These were assessed after 14 days. Following complication will be assed. Meningoencephalitis, Upper respiratory tract infection, Bronchopneumonia, Otitis media, Stomatitis, Malnutrition, Dehydration, Acute diarrhea, Vaccinated group, Non-vaccinated group. Outcome: Outcome was assessed in terms of recovery or death. Recovery: A child was said to be recovered when symptoms and signs disappeared, good oral intake assessed after 2 weeks of admission.

Death: Died due to any a fore mentioned complication during hospital stay.

METHODOLOGY

The study was conduc-ted at Pediatric Department, The Children Hospital and Institute of child's Health, Lahore, from 1st February, 2020 to 31st January, 2021.

This was Descriptive case series study while Non-probability consecutive sampling technique used.

Sample size of 198 was calculated using confidence level as 95% with absolute precision as 2% and expected prevalence of vaccination = 98%.[9]

Inclusion Criteria:

- Both Genders of 1-15 years of age
- Diagnosed with measles (as per operational definition).

Exclusion Criteria:

- Reported with comorbidities (known case of celiac disease/chronic diarrhea/or prior history of neurological problem)
- Non-specific rashes other than measles.

The data collection procedure was done after approval of Institutional Board Review (IRB and ethical committee of the hospital). Total 198 patients who fulfilled the inclusion and exclusion criteria were enrolled into the study after obtaining an informed written consent from the parents.

Demographics including age, sex, relevant history and physical examination (blood count, chest x-rays) were recorded for all the patients. Vaccination status was recorded and all these patients were observed about 2 weeks stay in hospital for complications of measles including pneumonia, oral ulcer, malnutrition, diarrhea, dehydration, inability to feed, otitis media and acute encephalitis and outcome was assessed in terms of recovery or death as per operational definition.

All the findings were recorded and analyzed using SPSS software v25.0. Statistics such as frequen-cies, means, standard deviations and percentages were used to describe all the variables. A p-value ≤ 0.05 was considered statistically significant. Mean and standard deviation was calculated for quantitative variables (age and weight) and qualitative variables (vaccinated, unvaccinated, respiratory tract infections, pneumonia, ulcers, malnutrition, otitis media, encephalitis, recovery and death), frequency and percentage were calculated. Qualitative variables were compared using Chi-square test. Data were stratified for gender, age and weight. Post-stratification, Chi-square test was applied taking p-value ≤0.05 as statistically significant.

RESULTS

Total 198 children with measles were selected for this study. There were 86(43.4%) males and 112 (56.6%) females. Mean age of the children was 8.7± 4.31 year. Age distribution of the patients was done and two groups were made, age group 1-6 years and age group 7-15 years, 111(56.1%) patients were in 1-6 years age group and 87(43.9%) were in 7-15 years age group. According to weight of child distribution, 131(66.2%) had weight <25 kg, while 67(33.8%) had weight >25 kg.

According to vaccination status, 131(66.2%) were vaccinated and 67(33.8%) were un-vaccinated. The encephalitis was significantly less in the vaccinated group (14.5%) as compared to un-vaccinated children (26.9%) with a p-value 0.035. The upper respiratory tract infection was insignificantly less in the vaccinated group (9.9%) as compared to un-vaccinated children (17.9%) with a p-value 0.109.

The bronchopneumonia was significantly less in the vaccinated group (10.7%) as compared to un-vaccinated children (28.4%) with a p-value 0.002. The otitis media was significantly less in the vaccinated group (5.3%) as compared to un-vaccinated children (14.9%) with a p-value 0.023. The stomatitis was significantly less in the vaccinated group (15.3%) as compared to un-vaccinated children (29.9%) with a p-value 0.016. The malnutrition was insignificantly less in the vaccinated group (10.7%) as compared to un-vaccinated children (20.9%) with a p-value 0.051.

The dehydration was significantly less in the vaccinated group (11.5%) as compared to un-vaccinated children (31.3%) with a p-value 0.001. The acute diarrhea was significantly less in the vaccinated group (5.3%) as compared to un-vaccinated children (20.9%) with a p-value 0.001. According to outcome distribution, mortality was observed in 5.3% patients with vaccination, while 14.9% patients died with un-vaccination with a p-value 0.023.

DISCUSSION

Measles is a highly contagious, serious disease caused by a virus and is one of the leading causes of death among young children even though a safe and cost-effective vaccine is available. Earlier diagnosis of measles in Pakistan were often based on the clinical measles case definition.[21-22] In Pakistan, where measles continue to be prevalent, cold chain maintenance is mandatory, since regular mixed epidemics and similar seasonality of both diseases with highest prevalence occurs from the month of March to May.[14]

Various surveys of itchiness and fever outbreaks in Bangladesh have recognized mixed outbreaks of measles and rubella, signifying that mixed outbreaks may be relatively common in the region. A study

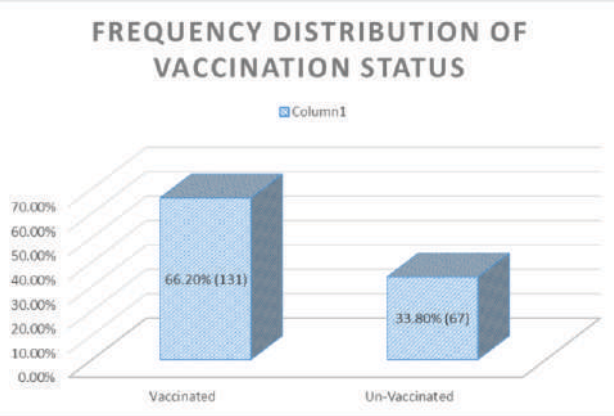

Table 1: Comparison of Encephalitis with Vaccination Status

Encephalitis	Vaccination status		Total	p-value
	Vaccinated	Un-vaccinated		
Yes	19 14.5%	18 26.9%	37 18.7%	0.035
No	112 85.5%	49 73.1%	161 81.3%	
Total	131 100.0%	67 100.0%	198 100.0%	

Table 2: Comparison of Upper Respiratory Tract Infection with Vaccination Status

Upper respiratory tract infection	Vaccination status		Total	p-value
	Vaccinated	Un-vaccinated		
Yes	13	12	25	0.109
	9.9%	17.9%	12.6%	
No	118	55	173	
	90.1%	82.1%	87.4%	
Total	131	67	198	
	100.0%	100.0%	100.0%	

recently conducted by WHO Integrated Management

Table 3: Comparison of Bronchopneumonia with Vaccination Status

Broncho-pneumonia	Vaccination status		Total	p-value
	Vaccinated	Un-vaccinated		
Yes	14 10.7%	19 28.4%	33 16.7%	0.002
No	117 89.3%	48 71.6%	165 83.3%	
Total	131 100.0%	67 100.0%	198 100.0%	

Table 5: Comparison of Stomatitis with Vaccination Status

Stomatitis	Vaccination status		Total	p-value
	Vaccinated	Un-vaccinated		
Yes	20 15.3%	20 29.9%	40 20.2%	0.016
No	111 84.7%	47 70.1%	158 79.8%	
Total	131 100.0%	67 100.0%	198 100.0%	

of Childhood illness for measles at Karachi found that measles was present in only 75% cases, and that many of so-called measles cases were of Dengue fever.[14,15]

The majority of our patients in both groups were between one to six years old which is similar to the various studies from abroad and within the country.[16-18] An important thing to note from these results is that nearly 50% of children in both groups (vaccinated and un-vaccinated) were less than 5 years of age. This indicates that many children of this age group are still

Table 6: Comparison of Malnutrition with Vaccination Status

Malnutrition	Vaccination status		Total	p-value
	Vaccinated	Un-vaccinated		
Yes	14 10.7%	14 20.9%	28 14.1%	0.051
No	117 89.3%	53 79.1%	170 85.9%	
Total	131 100.0%	67 100.0%	198 100.0%	

Table 7: Comparison of Dehydration with Vaccination Status

Dehydration	Vaccination status		Total	p-value
	Vaccinated	Un-vaccinated		
Yes	15 11.5%	21 31.3%	36 18.2%	0.001
No	116 88.5%	46 68.7%	162 81.8%	
Total	131 100.0%	67 100.0%	198 100.0%	

Table 8: Comparison of Acute Diarrhea with Vaccination Status

Acute diarrhea	Vaccination status		Total	p-value
	Vaccinated	Un-vaccinated		
Yes	7 5.3%	14 20.9%	21 10.6%	0.001
No	124 94.7%	53 79.1%	177 89.4%	
Total	131 100.0%	67 100.0%	198 100.0%	

Table 9: Comparison of Outcome with Vaccination Status

Outcome	Vaccination status		Total	p-value
	Vaccinated	Un-vaccinated		
Died	7 5.3%	10 14.9%	17 8.6%	0.023
Recovered	124 94.7%	57 85.1%	181 91.4%	
Total	131 100.0%	67 100.0%	198 100.0%	

unprotected. The possible reasons could be vaccine efficacy, interference of maternal antibodies with the vaccine and/or low vaccination coverage.

Vaccination at the age of 12-15 months and a booster dose of measles vaccine at 4-6 year of age can bring the disease under control in the future.[19] In our study malnutrition rate was not very high and overall 14.1% of the children were malnourished in both groups. These findings are in contrast to the other studies in which malnourished children experienced more severe measles infection at a greater frequency because of their altered immune response leading to widespread viral infections.[20] The previous studies from Pakistan had shown the incidence of severe malnourished with measles to be 41.33% 61 and 71%.[21,22]

Bronchopneumonia is a serious common complication of measles, which occurs in majority (10.7% and 28.4%) of children in vaccinated and un-vaccinated respectively in our study. It is one of the common complications in our study similar to that reported from various national and international studies.[23,24,25]

Diarrhea was another common complication having rate of 10.6%% in our study whereas it was also reported in some studies with more or less frequencies.[21-24] Other complications include upper respiratory tract infection, oral ulcer, dehydration, otitis media and encephalitis as 12.6%, 20.2%, 18.2%, 8.6% and 18.7% respectively. Few other studies have also reported more or less rate of similar these complications.[22-26]

In vaccinated group, complications include bronchopneumonia in 49 (49%), upper respiratory tract infection in 39 (39%), diarrhea in 32 (32%), ulcer in 31 (31%), dehydration in 15 (15%), otitis media in 10 (10%), malnutrition in 2 (2%), encephalitis in only 1 (1%) case. In non-vaccinated group, bronchopneumonia in 51(51%), diarrhea in 50 (50%), upper respiratory tract infection in 24 (24%), oral ulcer in 22 (22%), dehydration in 20 (20%), otitis media in 17 (17%), malnutrition in 12 (12%), and encephalitis in 11 (11%) patients.[13]

Measles is extremely contagious. Outbreaks in Europe remain common although fatalities are now rare; 12 deaths were reported in the European Union in 2005, 11 in Romania and one in Germany.[25] According to WHO's latest data, global deaths from measles have fallen from an estimated 873000 in 1999 to 345000 in 2005. In Africa, progress has been even greater, with deaths from measles falling by 75%, from an estimated 506000 to 126000.[26-28]

In many developing nations, however, case fatality rates range from 1 to 5%, and can reach 30% in refugee settings and among malnourished children. Despite there being a safe and effective vaccine available for over four decades, measles is still a leading cause of death for young children.[25]

CONCLUSION

The vaccination program in Pakistan for production of immunity against measles, is insufficient and the children who are vaccinated with measles vaccine before their first birthday should be considered unvaccinated and should receive two doses of measles vaccine according to the standard schedule. Vaccination at the age of 12-15 months and a booster dose of measles vaccine at 4-6 year of age can bring the disease under control in the future. Further investigation is needed.

Limitations of Study: It is among the few studies in

our setup about the complications of Measles in children's admitted in Pediatrics Department. Limitation of study is that its results can't be generalized over large geographic area because its data is collected from one Tertiary care hospital.

Ethical Approval: This study was approved by Ethical Review Committee of The Children's Hospital, Lahore.

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Conflict of Interests: There is no conflict of interests to be declared.

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ROLE OF ADJUVANT ZINC THERAPY IN PNEUMONIA IN PAEDIATRIC POPULATION

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Abstract

Background: Pneumonia is an important cause of illness and leading cause of death in young children in developing countries. More than 99% of pneumonia deaths occur in low- and middle- income countries (LMICs).

Objective: To compare mean time taken by each group for resolution of symptoms of pneumonia with and without zinc supplementation as adjuvant therapy in children admitted with pneumonia in referral hospital.

Methodology: This was a randomized controlled trial on 140 patients admitted in Paediatric Medicine Department, Akhter Saeed Hospital, Lahore from 10th july 2020 to 9th January 2021.All the patients were randomly distributed in two groups by lottery method. Group A: conventional treatment group of pneumonia as per standard management guidelines (oxygen inhalation, antibiotics (3rd generation cephalosporins 80mg/kg/day in 2 divided doses and nebulization. Group B. Standard treatment as above plus zinc supplementation (20mg zinc sulphate daily).

Results: Among 140 study cases, 83 (59.3%) were male while 57 (40.7%) were female patients. Mean age was 3.50 ± 1.16 years. Mean duration of disease was 8.45 ± 4.56 days: however, 75 % patients had illness for more than 7 days. Among study cases, 68 (48.6 %) mothers were illiterate and 72 (51.4 %) mothers were literate. Mean time taken for the resolution of symptoms in group A was found to be 49.64 ± 3.23 hours and in group B, mean time was found to be 41.37 ± 4. 1 hours. P=0.000.

Conclusion: The study results have found that resolution of symptoms was significantly earlier in study group compared to control group thus indicating zinc therapy to be effective, safe and reliable in treatment of pneumonia as adjuvant therapy. The clinicians may like to prescribe zinc supplementation as adjuvant therapy in treatment of pneumonia to achieve desired clinical outcomes thus decreasing ultimate morbidity and mortality.

Key Words: Zinc Supplementation, Pneumonia, Adjuvant therapy.

Acute respiratory tract infections (ARI) are the most common illnesses in childhood comprising of up to 50% of all illnesses in children less than 5 years old.[1] The burden of hospitalization for children with community-acquired pneumonia is very high especially among under 5 years old children.[2] It is one of the major causes of deaths in young children in developing countries, but early diagnosis and intervention can effectively reduce mortality[3]. It is reported that about 14.60% people die due to Influenza & Pneumonia in Pakistan among which two third of the population belong to pediatric age group[4]. There are many factors like infecting agents, environmental factors and host factors which determine the type, severity and frequency of respiratory tract illnesses. Amongst the host factors, the zinc deficiency has been associated with inadequate immune function and its supplementation in different diseases especially diarr-

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hea reflects its effectiveness as an adjunct therapy in the management of these diseases.[5] The role of zinc in the treatment of pneumonia has been explored in different studies but the results have shown conflicting findings.[6,7] However, Valvali et al reported effectiveness of zinc supplementation in the treatment of pneumonia among children with shorter time of recovery and resolution of symptoms i.e. 42.26 + 6.66 hours in the zinc groups vs. 47.52 + 7.15 hours in the placebo group.[8] The objective of the study was to compare mean time taken by each group for resolution of symptoms of pneumonia with and without zinc supplementation as adjuvant therapy in children admitted with pneumonia in referral hospital.

Pneumonia: children with findings of fast brea-thing and chest recessions on inspection of chest were labeled as having pneumonia. Fast breathing rate was defined as >50/ min in age group 2 month- 1 year, and rate>40/min in 1-5 years old children.

Severe Pneumonia: Children with any danger sign (unable to feed, vomits repeatedly, convulsions, lethargic or unconscious) or stridor in a calm state.

Time for resolution of pneumonia: the outcome in these children for both groups i.e. with and without zinc supplementation is time for 'resolution of symptoms' i.e. time taken in days from presentation in hospital till the resolution of symptoms in patients (normalization of respiratory rate and resolution of recessions). Complications arising in both groups during patient stay were also recorded.

Adjuvant Therapy: Treatment that is given in addition to the standard initial treatment.

METHODOLOGY

Study was conducted in the Department of Pediatric Medicine, Akhtar Saeed Trust Hospital Lahore. It was a randomized control trial. Random allocation in groups was done by lottery method.

Inclusion criteria:

Age 2 months to 5 years.

Both genders.

Children with pneumonia (as per operational definition) admitted to a referral hospital.

Exclusion criteria:

Patients with previous one or two episodes of wheezing determined on history.

Patients with severe pneumonia.

Patients with severe malnutrition (weight for age < 60th percentile).

Patients with congenital heart diseases and chronic lung disease determined on history and medical record.

Patients with history of taking zinc for any inter-current illnesses like diarrhea in the previous month prior to admission

History of taking immunosuppressive medica-tions (steroids) or chemotherapy.

Sample size was calculated using S-size software with total number of patients as 140; 70 in each group was calculated with 95% confidence interval, 80% power of test and taking magnitude of mean duration of time of recovery and resolution of symptoms i.e. 42.26 + 6.66 hours in the zinc groups vs. 47.52 + 7.15 hours in the control group.[6] It was a non probability consecutive sampling technique. A total 140 children presenting with pneumonia to the Pediatric department of Akhtar Saeed Teaching hospital Lahore and fulfilling the inclusion criteria were enrolled. An informed consent was obtained from the parents before inclusion in the study. Information regarding their demographic data (serial no, name, age, gender) was recorded in the proforma The cases were included on the basis of operational definitions of pneumonia after fulfilling inclusion / exclusion criteria. All the patients were randomly distributed in two groups by lottery method. Group A: conventional treatment group as per standard management guide-lines (oxygen inhalation, antibiotics 3rd generation cephalosporin (80mg/kg/day in 2 divided doses, nebu-lization) Group B: zinc supplementation (elemental zinc 20mg per 5ml) 2.5 ml in patients less than 6 months and 5ml in patients more than 6months was given and continued till discharge in addition to the conventional treatment. All the children were observed in the hospital for the time taken in resolution of the symptoms (as per operational definition). The results

were noted in the proforma as well and Confidentiality of the data was ensured.

Data was analyzed by using SPSS version 20. Numerical variables i.e. age and mean time for the resolution of symptoms for the two groups were summarized as mean and standard devia-tion. Qualitative variables like gender were presented in the form of frequency and percentages. Data was stratified for age and gender to control the effect modifier. The mean time of resolution of symptoms in the two groups was compared using independent sample t test and p value.

RESULTS

The study cases comprised of 140 patients meeting inclusion criteria of our study. Among them, 83 cases (59.3%) were male and 57 cases (40.7 %) were female (Table No. 1).

Mean age of study cases was 3.50 ± 1.16 years (ranging from 2 months to 5 years). Mean age of male cases was 3.54 ± 1.11 years and 3.44 ± 1.23 years in female cases (p=0.607). The vast majority of study cases 116 (82.9 %) were aged more than 2 years. (Table No. 2).

Mean duration of diseases before admission was 8.45±4.56 days and 105 cases (75%) had duration of illness more than 7 days (Table 3).

Mean time taken for the resolution of symptoms of pneumonia in group A was found to be 49.64 ± 3.23 hours while in group B, mean time was noted to be 41.37 ± 401 hours (Table 4).

Table 1: *Distribution of Study Cases According to Sex. (n = 140)*

Gender	Group A		Group B	
	Fre-quency	Per-centage	Fre-quency	Per-centage
Male n = 83 (59.3 %)	43	61.4	40	57.1
Female n= 57 (40.7 %)	27	38.6	30	42.9
Total	**70**	**100**	**70**	**100**

Mean duration of resolution of symptoms of pneumonia was stratified with regards to gender (Table 5)

DISCUSSION

Childhood pneumonia is an important cause of illness and leading cause of death low- and middle-income countries (LMICs).[9] The recent estimate is a median incidence of 0.22 episodes per child year (e/cy) with severe pneumonia contributing to 11.5%

Table 2: *Distribution of Study Cases According to Age. (n = 140)*

Age groups (n=140)	Group A		Group B	
	Frequency	%	Frequency	%
Up to 2 Years n= 24 (17.1 %)	09	12.9	15	21.4
More than 2 years n= 116 (82.9 %)	61	87.1	55	78.6
Total	**70**	**100**	**70**	**100**

Table 3: *Distribution of Study Cases According to Duration of Disease(n = 140)*

Disease duration (n=140)	Group A		Group B	
	Frequency	%	Frequency	%
Up to 7 days (35) (25.0 %)	19	27.1	16	22.9
More than 7 days (105) (75.0 %)	51	72.9	54	77.1
Total	**70**	**100**	**70**	**100**

Table 4: *Distribution of Cases according to Mean Time Taken for Resolution of Symptoms (n = 140)*

Group A (In hours)		Group B (In hours)	
Mean	**+/-SD**	**Mean**	**+/-SD**
49.64	3.32	41.37	4.01
P=0.000			

Table 5: *Stratification of Gender with Regards to Mean Time taken for Resolution of Symptoms in Both Groups. (n = 140)*

Gender	Groups	Time		P – value
		Mean	SD	
Male (n=83)	**Group A** (n=43)	50.00	3.45	**0.000**
	Group B (n=40)	41.05	4.44	
Female (n=57)	**Group A** (n=27)	49.07	2.82	**0.001**
	Group B (n=30)	41.80	3.37	

in LMICs.[10,11] The leading bacterial cause of pneumonia in developing countries is pneumococcus (30–50%), H. influenzae type b (10–30% of cases), S. aureus and K. pneumoniae. Empiric antibacterial selection for treatment of childhood CAP must be based on age and the likely causative organisms. Early and prompt diagnosis of bacterial pneumonia is lacking in most of the developing countries, hence empirical treatment is usually practiced.[12]

Our study comprised of a total of 140 patients meeting inclusion criteria of our study. Of these 140 study cases, 83 (59.3 %) were male patients while 57 (40.7 %) were female patients. Sakellaropoulou et al reported 59 % boys with pneumonia which shows similar trends of male gender predominance compared to our study results.[13] Boloorsaz et al et al reported 48.4% boys among all study cases with pneumonia.[14] Wrotek et al also reported male gender predominance which is same as that of our study results.[1]. Duru et al reported similar results.[16]

Mean age of our study cases was 3.50 ± 1.16 years (with age range 1-5 years). Mean age of the male patients was noted to be 3.54 ±1.11 years compared to 3.44 ± 1.23 years in females (p=0.607). Majority of our study cases i.e. 116 (82.9 %) were aged more than[2] years. Boloorsaz et al found mean age of children with pneumonia as 4.7 ± 5 years which is close to our findings.[14] Sakellaropoulou et al reported mean age 4.67 ± 0.39 years among study cases similar to our series.[13]

Mean duration of symptoms before hospitalization was 8.45±4.56 days and 105 cases (75 %) had duration of illness more than 7 days. Boloorsaz et al from Iran reported mean duration of symptoms as 10.8 days which appears close to our results.[14] Sakellaropoulou et al had reported similar findings.[13]

Mean time taken for the resolution of symptoms of pneumonia in group A was 49.64 ± 3.23 hours compared to 41.37 ± 4. 1 hours in group B. Valvali et al reported effectiveness of zinc supplementation in the treatment of pneumonia among children with shorter time of recovery and resolution of symptoms i.e. 42.26 +/-6.66 hours in the zinc groups vs. 47.52 +/-7.15 hours in the placebo group.[17] These findings are consistent with our study results.

CONCLUSION

Zinc supplementation as adjuvant therapy in cases of childhood pneumonia was found to be effective, in early resolution of symptoms of pneumonia as mean duration of resolution of symptoms was significantly lower in study group. Our study was limited to one center with small sample size. Large scale multicenter randomized trials are indicated for final opinion. The recommendation may be passed on to clinicians treating these cases to consider adding zinc supplementation as adjuvant therapy in cases of childhood pneumonia. This may prove beneficial on long term basis.

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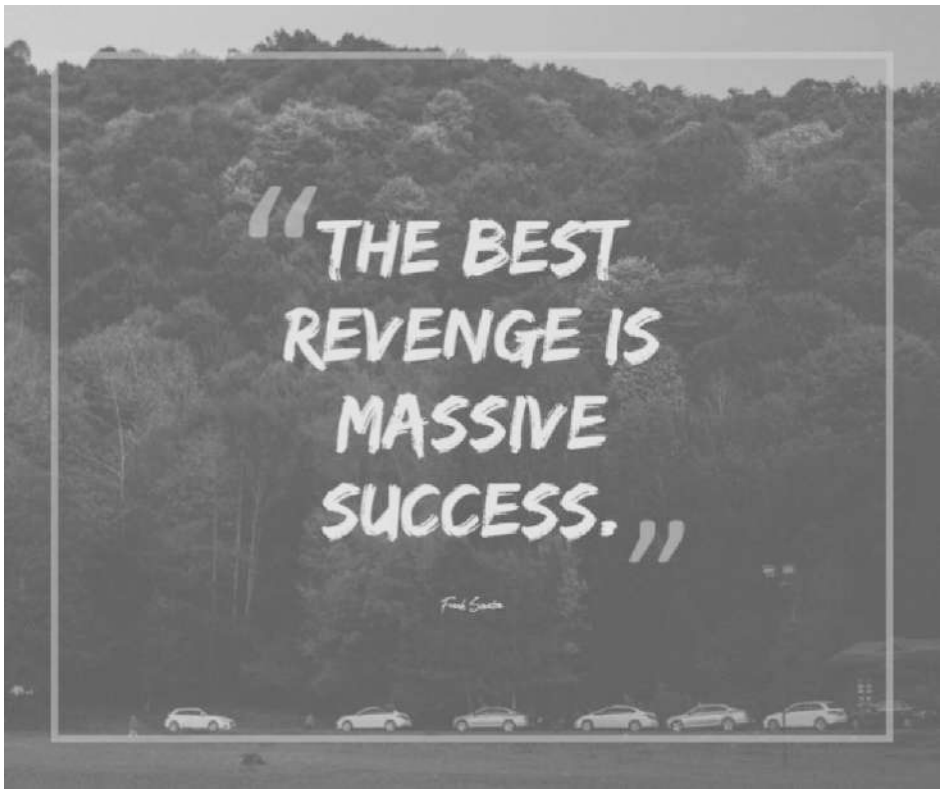

ASSAULT / VIOLENCE AMONG MEDICAL PROFESSIONALS DURING THEIR WORK

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Abstract

Background: Violence against medical community including doctors, nurses and paramedical staff is at a rise in the recent past. Hospitals are places where sick people get benefit, sometime due to unfavorable circumstances the staff working in the hospital is subject to physical or non-physical violence which not only discourages but also demotivates the staff. Violence against doctors and paramedical staff is mostly due to unsatisfied patients and their relatives, who have multiple reasons for such acts. Whatever, the reason may be it produces apathy, loss of interest in the work among medical community. Such violence is observed among the medical staff who spend most of their time with the patient such as paramedical staff. Consultant doctors who visit the patient once or twice a day encounter such incidences to a lesser extent. Majority of such unpleasant events could be prevented through good security measures and proper management.

Methodology: It was a cross-sectional study conducted at D.H.Q Sheikhupura.

Results: Results exhibited physical and non-physical violence among all categories of medical community. However, such violence is more common among the paramedical staff. Doctors also face violence which is mostly non-physical in nature. Whatever, the nature of violence maybe, majority of such cases could be prevented through good management and security measures.

Conclusion: The staff working in the emergency department of the hospital is most vulnerable to violence. Among all the staff, the junior doctors and nurses due to lack of experience and no proper training to encounter such incidences are at the top of the list. Violence in the emergency department is due to multiple factors, majority of which could easily be prevented through good management and administration. A uniform policy should be devised by all the stakeholders to minimize all negative events which produces a sense of insecurity among the staff working in the emergency department of hospitals.

Key Words: Assult, Violence, medical, professionals

Violence against medical professionals which include doctors, nurses, paramedical staff and administrative staff is observed worldwide and Pakistan is no exception.[1-4]

Hospitals are designed to benefit the community by providing treatment to ailment of the suffering. Patients from different diseases are getting benefits from the hospitals.[5] Majority of the hospitals has got different sections such as surgical unit, medical unit, emergency unit etc to cater different patients. When the suffering for which patient is admitted to the hospital is settled he leaves the hospital without passing any favorable remarks, but if something goes contrary to the expectations of the patient or his attendants they usually become aggressive against the hospital staff and in particular doctors and exhibit violent behaviors.[6]

Although such aggression is observed anywhere in the hospital, but the most common place where such behavior is observed is the place of first interaction i.e. the emergency unit of the hospitals.[7,8]

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Emergency department of any hospital has a high potential for violence against the staff working there. The nature of the work in this particular department makes it a potential threat for the workers.[9]

Emergency department is heavily loaded with updated equipment and staff to manage any emergency situation. In the emergency department, majority of the hospitals in our setting has maximum staff during the morning shift, the staff during evening and night shifts usually is less in number and also not so senior in rank which invites to such violence against the working staff during these hours, majority of such incidences could be prevented through good administration only.

METHODOLOGY

The aim of the study is to explore the matter deeply about workplace violence experienced by staff members working in the emergency department of District Headquarter Hospital, Sheikhupura. This judgment admits degree and character of violence and the causes for such violence in the emergency department. It is a cross sectional study. It inquired multiple character of violence against staff members working in the emergency department of (DHQ) District Head-quarter Hospital, Sheikhupura. Study was carried in the emergency department of District Headquarter Hospital, Sheikhupura. The study population included all the staff members working round the clock in the emergency department, which comprised of 70 doctors, 108 nurses, 44 administrative and paramedical staff members. A self-designed questionnaire was used to collect data, which was validated through a pilot study, appro-priate changes were made through this pilot study in another hospital and then it was used for the study. The questionnaire comprised of issues pertinent to the features of the participants, the cause and frequency of vulnerability to violence in the yesteryear, perceived cause and impact on workers and preventive measures taken by hospital for such violence. The questions were open ended and multiple choice questions.

Data was analyzed through SPSS. Features of participant and their vulnerability to violence was analyzed through descriptive statistics. To assess the association between physical and nonphysical violence and participant characteristics chi square (χ^2) tests were used. P <0.05 was accepted as statistically significant in all analysis.

RESULTS

A total of 222 personal participated in the study which included doctors, nurses and paramedical staff. 76.8% of the participants were male and 23.2% were females, among them 31.98% were doctors, 36.03 were nurses and 31.98% were paramedical staff members.

Less than 50% i.e. 47.29% were less than 30 years of age whereas 52.70% were above the age of 30 years. 56.30% had less than 5 years of experience in the emergency department, 24.77% had experience between 5-10 years and 18.9% had more than 10-year work experience in the emergency department.

Table 1: Characteristic of Participants (n=222)

Characteristic	*F*	%age
Gender		
Male	170	76.8
Female	52	23.2
Age		
⩽30 years	105	47.29
>30 years	117	52.70
Nature of Job		
Doctor	71	31.98
Nurse	80	36.03
Paramedical Staff	71	31.98
Experience in Emergency Department		
<5 years	125	56.30
5-10 years	55	24.77
⩾10 years	42	18.9
Education		
<Bachelor	150	67.56
⩾Bachelor	72	32.43

Total of 17.56% reported physical violence whereas 35.5% reported non-physical violence. Visitors were involved in 32.43% of the physical violence and 18% of non-physical violence. Patients involvement in physical violence is 16.66% of the cases whereas non-physical violence caused by patients was 23.42%. Physical violence caused by colleagues

Table 2: Violence Characteristic

Feature of violence	Physical		Non-physical	
Vulnerability of violence during study period				
	F	**%**	***F***	**%**
Yes	39	17.56	79	35.5
No	74	33.3	30	13.5
Culprits of violence				
Families/visitors	72	32.43	40	18
Patients	37	16.66	52	23.42
Colleagues	7	3.15	14	6.30
Need for treatment after violence				
No treatment required	6	2.70	8	3.60
Self-treatment	90	40.54	79	35.58
Needed treatment but did not receive	12	5.40	16	7.20
Treated by other professionals	4	1.80	7	3.15
Causes of violence				
Waiting time	13	5.40	3	1.35
Lack of violence prevention measures	18	8.10	28	12.61
Unmet expectations of patients&families	17	7.65	23	10.36
Non availability/lack of medicine	14	6.30	18	8.10
Anxiety/ fear/ stress	12	5.40	13	5.85
Mental illness	9	4.05	11	4.95
Staff attitude	20	9.0	8	3.60
Influence of illness/pain	6	2.70	5	2.25
Lack of people awareness	4	1.80	7	3.15
Under influence of drug	3	1.35	3	1.35
No reason	2	0.90	5	2.25

was 3.15% and non-physical violence was 6.30%.

5.4% of physical violence and 7.2% of non-physical violence cases required treatment but due to multiple reasons did not received any treatment.

2.7% of physical violence and 3.6% of non-physical violence did not required any treatment. 41.54% of physical violence cases and 35.58% cases of non-physical violence cases treated themselves. 5.4% of physical violence and 7.2% of nonphysical violence medical professionals required medical treatment but due to multiple reasons did not received any treatment. 1.8% of physical violence and 3.15% of nonphysical violence cases were treated by other health professionals.

Prolonged waiting hours resulted in 5.4% of physical violence and 1.35% of non-physical violence cases. Lack of preventive measures resulted in 8.1% of physical violence and 12.61% of non-physical violence cases. Patient and relatives of the patient expectations not fulfilled resulted in 7.65% of physical and 10.36% of non-physical violence. Non availability of medicine resulted in 6.30% of physical and 8.10% of non-physical violence. Emotional factors such as anxiety, fear resulted in 5.4% and 5.85% of physical and non-physical violence. Mental illness resulted in

Table 3: Violence (Physical and Non-Physical) Exposure

	Physical				Non-physical			
	F	**%**	X^2	***P* value**	***F***	**%**	X^2	***P* value**
Gender								
Male	70	31.53	1.22	0.18	93	41.89	0.08	0.332
Female	18	8.10			41	18.46		
Age								
⩽30 years	44	19.8	2.79	0.009	73	32.88	0.088	0.337
>30 years	35	15.76			70	31.53		
Job category								
Doctor	21	9.45	2.25	0.05	46	20.7	3.13	0.007
Nurse	32	14.41			48	21.62		
Paramedical Staff	41	18.46			34	15.31		
Experience in Emergency Department								
<5 years	45	20.27	2.33	0.043	80	36.03	3.65	0.012
5-10 years	23	10.36			41	18.46		
⩾ years	11	5.85			20	9.0		
Education								
<Bachelor	29	13.06	1.024	0.075	50	22.52	0.304	0.216
⩾Bachelor	50	22.5			93	41.89		

Table 4: Nature of Job and Prevalence of Violence

Types of effects	Doctors	Nurses	Paramedical Staff	Overall
	F (%)	F(%)	F(%)	F(%)
Reduced communication, impinging with patient / relatives	63(28.37)	38(17.11)	23(10.36)	98(44.14)
Hopelessness/ disappointment	73(32.88)	42(18.91)	25(11.26)	82(36.93)
Minimize time of patient care	66(29.72)	35(15.76)	19(8.55)	102(45.94)
Fear and anxiety	12(5.40)	60(27.02)	40(18.01)	110(49.54)
Beneficial decisions that involve risk are avoided	68(30.63)	25(11.26)	14(6.30)	115(51.80)
Feeling to take revenge	72(32.43)	29(13.06)	33(14.86)	88(38.63)
Feeling of guilt	4(1.80)	96(43.24)	20(9.0)	102(45.94)
No impact on me	29(13.06)	30(13.51)	74(33.3)	89(40.09)

4.05% and 4.85% of physical and non-physical violence. Attitude of the staff resulted in 9% and 3.6% of physical and non-physical violence. Influence of disease on the patient resulted in 2.7% and 2.25% of physical and non-physical violence. Unawareness, drug influence and no obvious reasons resulted in minimal physical and non-physical violence on the medial professionals.

Males were exposed to 31.53% (p = 0.18) and 41.89% (P=0.332) to physical and non-physical violence, as compared to females who were exposed to 8.1% and 18.46% times to physical and non-physical violence. 91.8%(P=0.009) and 32.88%(P=0.337) time physical and non-physical violence was exposed to people less than 30 years of age, whereas physical and non-physical violence exposed to people more than 30 years of age was 15.76% and 31.53%. Doctors have to face physical violence in 9.4%(P=0.05) of the cases whereas non-physical violence was faced in 20.7%(P=0.007) of the cases. Nurses has to face 14.41% physical violence and 21.62% non-physical violence. Paramedical staff faced 18.46% physical violence and 15.31% non-physical violence.

After the violence act, overall 44.14% of the whole staff minimized their communication and contact with the families. 36.93% of the staff were quite hopeless and disappointed about the future. 45.94% of the staff reduced their time of care with the patients. 49.54% of the staff had fear dealing with the patients. 51.80% of the staff was reluctant in taking decisions for their patients. 38.63% of the staff had a revengeful feeling. 45.94% of the staff had a feeling of guilt. 40.09% of the staff had no feeling and were quite normal after the incidence.

DISCUSSION

The study demonstrated a high preponderance of violence among the medical staff working in the emergency department of District Headquarter Hospital, Sheikhupura. Among the female staff, sexual harassment was found to be lower than other studies which is supported by Çelik Y, Çelik SŞ study conducted in 2007(10). Studies conducted by Phillips SP, Schneider MS and Firth-Cozens J in 1993 and 1990, are of the same view that, sexual harassment issues have not been deeply investigated among female workers of the hospital because they are reluctant to respond to such studies and fear of being exposed to the community.[11,12]

This study supports the finding that in majority of the cases, both physical and non-physical violence against medical staff is by the relatives / attendants of the patient, sometime patient themselves are involved in such violence in a small proportion, a study conducted in china in 2012 by Hesketh T, Wu D, Mao L, Ma N supports this study, another study conducted by Wu D, Wang Y, Lam KF, Hesketh T in china in 2014 is also in favour of this study.[13,14]

A study conducted in a Saudi University Hospital in 2016 by Alkorashy HAE, Al Moalad FB and another study conducted by Shahzad A, Malik R in Pakistan in 2014, supports the current study that violence among the co-workers which is a worrying issue and needs to be discussed, it is mainly related to stress and anxiety attributed to sensitive nature of the work.[15,16]

Doctors are facing non-physical violence which

mainly includes abuse and threats of serious nature as compared to non-doctors who are facing more physical violence which require treatment, it is supported by Hobbs FR, Keane UM in 1996 and another study done by Ayranci U in 2004.[2,8] Physicians are facing non-physical violence from dissatisfied patients and their relatives, however staff nurses and paramedical staff are facing physical violence. There were no obvious gender differences for any type of violence.

It is also observed that violence cases are reported among young, untrained staff members of the emergency department. Long waiting hours by the patient and their families make them vulnerable against doctors. Senior medial staff particularly physicians due to their experience resolves such issues which junior doctors lack, it is supported by study conducted in 1995 by Grant D and another study conducted in 2000 by Derlet RW, Richards JR.[17,18]

The long waiting time of the patients which make them vulnerable to violence can be resolved through better management and proper utilization of the available resources. As emergency department of any hospital is the most sensitive department, the chain of supply of medicine in this particular department have to be managed adequately than the rest of the hospital. This not only gives confidence to the patient but also keep the families of the patient calm and satisfied, it is supported by Razzak JA, Hyder AA, Akhtar T, Khan M, Khan UR, study conducted in 2008 and another study conducted by Cham M, Sundby J, Vangen S in 2009.[19,20]

A study conducted in 2014 by Yao S, Zeng Q, Peng M, Ren S, Chen G, Wang J and another study conducted by Stathopoulou H in 2007, supports the view that protection of the working staff in the emergency department of the hospital is the responsibility of the management. Proper security measures, security alarms, cameras etc in proper working condition can minimize a large number of the violence cases.[21,22]

Study conducted by Gates DM, Ross CS, McQueen L in 2005 and another study conducted in 2006 by Ergün FŞ, Karadakovan A supports this view. Experience have advocated that proper training of the emergency staff to face undue circumstances through a variety of education programme, workshops and training to deal with patients and their families while working in the emergency department can provide well equipped emergency medical staff, which shall be capable to counter all circumstances which lead to violence in the emergency department.[23,24]

A study conducted in 2006 by Kwok R, Law Y, Li K, Ng Y, Cheung M, Fung V, et al and another study conducted in 2002 by Keely BR in 2002 supports the view that the prevalence of violence among the emergency staff is quite extensive, but majority of the time events are not reported which misleads the graveness of such incidences. The staff which is being victimized and not reporting the incidences properly have a view that reporting of such incidences will not produce any benefit and perceive it as part of their job. The best strategy in all such cases is that proper follow-up of the case should be done, protection should be provided to the reporting person. Culprit should be highlighted and proper feedback should be given to the reporting person, this shall build confidence among the rest of the staff members.[25,26]

Majority of the staff members top of which are doctors and nurses, after such incidences become depressed and plan to change their job to some other hospital excluding the emergency department. It is the responsibility of the administration of the hospital to build confidence among their emergency staff so that they shall not feel unprotected and insecure, such demotivating factor is supported through studies conducted by Gabe J, Ann Elston M in 2007, Burnham GM, Lafta R, Doocy S in 2009 and Yao Y, Wang W, Wang F, Yao W in 2014(27-29).

CONCLUSION

The staff working in the emergency department of the hospital is most vulnerable to violence. Among all the staff, the junior doctors and nurses due to lack of experience and no proper training to encounter such incidences are at the top of the list. Violence in the emergency department is due to multiple factors, majority of which could easily be prevented through

good management and administration. A uniform policy should be devised by all the stakeholders to minimize all negative events which produces a sense of insecurity among the staff working in the emergency department of hospitals.

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DENTAL ANXIETY AND ITS ASSOCIATION WITH SELF-ASSESSED DENTAL STATUS AND TREATMENT NEEDS AMONG ADULT PATIENTS

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Abstract

Background: Dental anxiety remains a leading problem that affects the adult patients. It causes negative attitudes towards getting dental therapy; thus, these patients live along with dental issues for an extended period.

Objective: The objective of the study is study to assess the dental anxiety and its association with self-assessed dental status and treatment needs among adult patients.

Methodology: It was cross-sectional study in which 150 patients visiting dental OPD of Sheikh Zayed Hospital, Lahore were included. The patient aged 18-50 years were included in the study. For data collection, a questionnaire was utilized, which consisted of questions on the self-assessment of dental status and frequency of tooth-brushing habits along with Corah's MDAS questionnaire to assess dental anxiety.

Results: Among 150 patients, 54.0% were females and the mean age of the patients was 30.31+15.98 years. Majority (60.0%) had satisfactory dental status as self-assessed by them and 48.0% needed little dental treatment according to their self-assessment. Among these patients, 88.0% (36.0% moderate anxiety, 22.0% high anxiety and 30.0% extreme anxiety) had dental anxiety while 12.0% had no anxiety.

Conclusion: Study concluded that dental anxiety was prevalent among majority of the patients and it has significant association with self-assessed dental status and dental treatment needs of adult patients.

Key Words: Dental status, dental anxiety, adults, self assessed, treatment needs

Oral health is considered an important part of general well-being and a significant public health issue.[1,2] In spite of developments in the dental equipments, dental materials and enhanced awareness[3] regarding oral health, dental anxiety remains a leading problem that affects the adult patients.[4] Anxiety is described as "state of an unpleasantness with related fear of danger from within/or a learned process of one's own environment".[5,6] Terms such as fear and phobia are often used synonymously with anxiety.[7]

Dental anxiety has been recognized as a common condition.[8] Anxiety related to dental care is placed fourth between ordinary fears while 9th among severe fears.[9] Its prevalence can be seen across all age groups.[10] An elevated portion of elderly patients experience mild-severe dental anxieties. According to an estimation almost 3 to 16 percent adults experience dental phobia.[11] It was evaluated that among Americans, 80% had some types of anxiety about dental treatment while 5 to 14 percent of them had severe dental anxiety.[12] According to the recent study conducted in Pakistan; the reported prevalence of dental anxiety was 6.1%.[13]

The etiology of dental anxiety is a multidimensional real or imaginative stimulus that leads to development of fear.[14] It differs from individual to individual but related to gender, age, customs, educational and socioeconomic levels.[15] It may also be linked with other attributes such as previous history

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of traumatic dental experience, personality of patient, and childhood experience of dental pain along with experience of a dental visit by a close friend or family member with a DA problem.[16]

Dental anxiety causes negative attitudes towards getting dental therapy; thus, these patients live along with dental issues for an extended period. Indeed nervous dental patients undergo additional dental ailments, simply as they delay or cancel their dental visit and thus make difficult their disease state. Hence, an anxious patient is mostly unable to maintain his good life quality due to his oral health condition.[17]

Dental anxiety is not only an issue for dental patients but also for dental professionals; and most of the times it makes dental treatment much difficult to be completed successfully.[18] Generally, the dentists ignore the problem of dental anxiety among patients visiting their clinics for dental problems treatment. Among patients, to assess dental anxiety a screening technique was utilized just by 20 percent dentists. For correct management alternatives in patients with dental problems, it is significant that dental professionals must examine the patients prior to starting the therapy. Regarding this purpose, several scales are utilized such as CDAS (Corah's Dental Anxiety Scale), DFS (Dental Fear Survey) and Modified Dental Anxiety Scale (MDAS). Therefore, to manage appropriately the nervous patients, it is important to assess the anxiety level before initiating the treatment.[19]

The MDAS is most commonly utilized for the measurement of anxiety. It was adapted from original CDAS. The MDAS benefit is due to its briefness, it is easy, simple to complete, and could be utilized like a cost-effective tool regarding population-based study.[20] It is a brief five-item questionnaire. Each item has five answers; the answers vary from "not anxious" scored 1 to "extremely anxious" scored 5. It is a straightforward and easy to complete and requires less time for finishing. Filling of the questionnaire does not increase patient anxiety, and has been shown to decrease anxiety in clinical settings. It has been established as trustworthy and valid cross-culturally, and hence has been interpreted in several languages.[21]

Limited number of studies has been performed in Pakistan so far that investigated the dental anxiety among patients. Therefore, it is pertinent to conduct a study to assess the dental anxiety and its association with self-assessed dental status and treatment needs among adult patients in Pakistan.

METHODOLOGY

It was cross-sectional study in which 150 patients visiting dental OPD of Sheikh Zayed Hospital, Lahore were included. The patient aged 18-50 years were included in the study. Patients with neuro-psychological symptoms and pregnant women were excluded from study.

The MDAS questionnaire is a validated tool and used to assess the dental anxiety during study. It is comprised of 5 questions related to feelings; if patient went to dental treatment tomorrow, waiting for treatment in waiting room, if patients were about to have tooth drilled, about to have scaling and polishing treatment and finally patient was about to have given local anesthetic injection in gum or on posterior teeth. All five questions have 5 responses. The total score of this scale ranges from 5 to 25 (1–5: not anxious), 6–10: low anxiety, 11–14: moderate anxiety, 15–18: high anxiety and 19–25: extreme anxiety/phobic).

For data collection, a questionnaire was utilized, which consisted of questions on the self-assessment of dental status and frequency of tooth-brushing habits along with Corah's MDAS questionnaire to assess dental anxiety. Approval from hospital ethical committee was obtained. Consent from patients was also obtained before data collection and confidentiality of data was ensured. The data was analyzed using SPSS version 24.0. Descriptive frequencies and chi-square test was used. Statistical significance was defined at P value <0.05.

RESULTS

Table-1 describes that among 150 patients, 97 (64.7%) were 18-30 years old while 53 (35.3%) were 31-50 years old. The mean age of the patients was 30.31+15.98 years.

Out of 150 patients, 69 (46.0%) were male and 81 (54.0%) were females.

Table 1: *Frequency Distribution of Patients According to Socio-Demographic Characteristics*

	Frequency	Percentage (%)
Age		
18-30 yrs	97	64.7
31-50 yrs	53	35.3
Total	150	100.0
Mean ± SD	30.31±15.98	
Gender		
Male	69	46.0
Female	81	54.0
Total	150	100.0

Table-2 exhibits that among 150 patients, 9(4.0%) said they never brushed while 86 (57.3%), 35(23.4%) and 23(15.3%) patients said they brush their teeth once, twice and thrice or more daily, respectively.

Among these patients, 54(36.0%) had last dental visit in less than one year, 47 (31.3%) between 1 to 3 years and 49 (32.7%) had last dental visit in more than 3 years.

Table 2: *Frequency Distribution of Patients According to Oral Behaviour and Self-Assessed Dental Status*

	Frequency	Percentage (%)
Frequency of tooth brushing		
Never	6	4.0
Once	86	57.3
Twice	35	23.4
Thrice or more	23	15.3
Total	150	100.0
Last dental visit		
Less than 1 yr	54	36.0
1 to 3 yrs	47	31.3
More than 3 yrs	49	32.7
Total	150	100.0
Self-assessed dental status		
Good	22	14.7
Satisfactory	90	60.0
Bad	38	25.3
Total	150	100.0
Self-assessed dental treatment needs		
Very much	21	14.0
Little	72	48.0
Not at all	17	11.3
Don't know	40	26.7
Total	150	100.0

Out of 150 patients, 22 (14.7%) had good dental status while majority 90(60.0%) had satisfactory and 38(25.3%) had bad dental status as self-assessed by them.

Table further describes that among 150 patients, 21(14.0%) needed dental treatment very much according to their self-assessment, 72 (48.0%) little, 17 (11.3%) not at all and 40 (26.7%) patient had no knowledge.

Table-3 demonstrates that among 150 patients, 18(12.0%) were not anxious, 54 (36.0%) patients had moderate anxiety and 33 (22.0%) had high while 45 (30.0%) patients had extreme anxiety.

Table-4 depicts significant association between self-assessed dental status and dental anxiety level (P=0.014).

Table-5 shows significant association between self-assessed dental treatment needs and dental anxiety level (P=0.005).

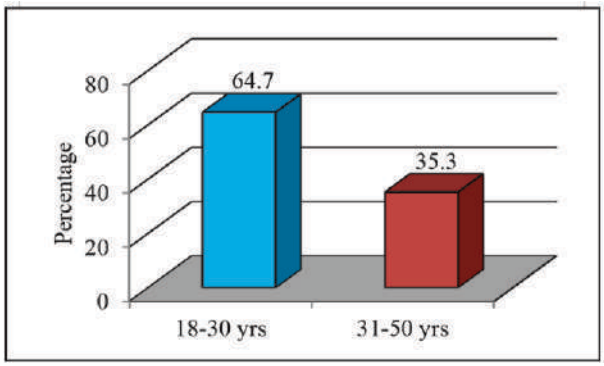

Figure-1: *Frequency Distribution of Patients According to Age*

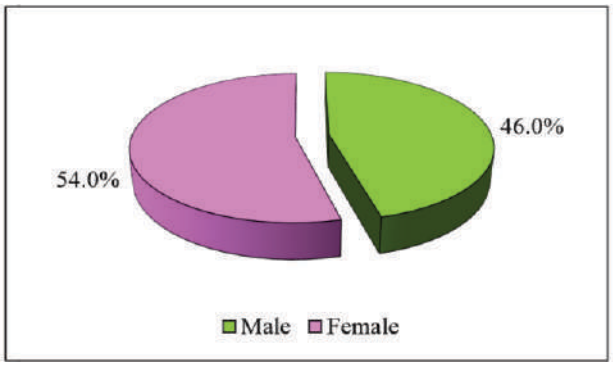

Figure-2: *Frequency Distribution of Patients According to Gender*

Table 3: *Frequency Distribution of Patients According to Dental Anxiety Status*

	Frequency	Percentage (%)
Non-anxious	18	12.0
Low anxiety	0	0.0
Moderate anxiety	54	36.0
High anxiety	33	22.0
Extreme anxiety	45	30.0
Total	150	100.0

Table 4: *Association between self-Assessed Dental Status and Dental Anxiety Level*

Self-assessed dental status	Dental anxiety level				Total
	Non	Moderate	High	Extreme	
Good	3 (2.0%)	9 (6.0%)	4(2.7%)	6 (4.0%)	22(14.7%)
Satis-factory	10 (6.7%)	33 (22.0%)	24 (16.0%)	23 (15.3%)	90(60.0%)
Bad	5 (3.3%)	12 (8.0%)	5(1.3%)	16(10.7%)	38(25.3%)
Total	18 (12.0%)	54 (36.0%)	33 (22.0%)	45 (30.0%)	150 (100.0%)

P-value = 0.014

Table 5: *Association between Self-Assessed Dental Treatment Needs and Dental Anxiety Level*

Self-assessed dental treatment needs	Dental anxiety level				Total
	Non	Moderate	High	Extreme	
Very much	3(2.0%)	8(5.3%)	5(3.4%)	5(3.3%)	21(14.0%)
Little	9 (6.0%)	26 (17.3%)	19 (12.7%)	18 (12.0%)	72 (48.0%)
Not at all	3(2.0%)	7 (4.7%)	1(0.6%)	6 (4.0%)	17(11.3%)
Don't know	3 (2.0%)	13 (8.7%)	8 (5.3%)	16 (10.7%)	40 (26.7%)
Total	18 (12.0%)	54 (36.0%)	33 (22.0%)	45 (30.0%)	150 (100.0%)

P-value = 0.005

DISCUSSION

Dental anxiety is a most significant problem among adult patients. In spite of developments in the dental equipments, dental materials and enhanced awareness regarding oral health, dental anxiety remains a leading problem that affect the adult patients. Therefore, current study was conducted to assess the dental anxiety and its association with self-assessed dental status and treatment needs among adult patients in Pakistan. To obtain proper results, a group of 150 patients was included in the study and found that most of the patients (64.7%) were 18-30 years old and 35.3% were 31-50 years old while the mean age of the patients was 30.00±15.98 years. The findings of our study are almost comparable with a study carried out by Fayad and teammates (2017) who reported that mean age of patients was 32.2 years.[21]

As far as gender of the patients is concerned, study revealed that more than half (54.0%) of the patients were females. Similar results were also reported by a study carried out by Dou and fellows (2018) that mainstream (53.1%) of patients were females.[11] But the finding of a study done by Sinha and comrades (2019) elucidated that males patients were in majority (58.0%).[6]

Regular brushing plays an important role in preventing people from oral diseases. Study indicated that 4.0% patients never brushed. Among the patients, 57.3% brushed their teeth once daily, followed by twice daily (23.4%) and thrice daily or more (15.3%). The findings of our study are comparable but exhibited better scenario than a recent study undertaken by Aliuddin and coworkers (2021) who confirmed that 30.8% patients never brushed while 38.6% patients brushed their teeth once daily, followed by twice daily (23.7%) and thrice daily or more (6.8%).[22]

Study disclosed that 36.0% patients had last dental visit in less than one year, 31.3% between 1 to 3 years and 32.7% had last dental visit in more than 3 years. A similar study carried out by Syed and associates (2013) highlighted that 36.0% patients had last dental visit in <1 year and 22.9% between 1 to 3 years while 13.2% patients had last dental visit in more than 3 years.[23] In our study only 14.7% patients had good dental status while majority (60.0%) had satisfactory and 25.3% patients had bad dental status as self-assessed by them but the results of a study done by Dou and fellows (2018) showed that 23.1% patients had good dental status, 41.5% had satisfactory and 35.4% patients had bad dental status as self-assessed by them.[11] Another study performed by Munir and collaborators (2018) indicated that 45%

patients had good while majority (55.0%) had poor dental status.[24] The results of our study further disclosed that 14.0% patients needed dental treatment very much according to their self-assessment, 48.0% little and 11.3% not required at all while 26.7% patient had no knowledge. The results of a similar study undertaken by Aliuddin and coworkers (2021) highlighted that 27.2% patients required dental treatment and 28.0% not required while majority (44.8%) of the patients were not aware about it.[22]

When the dental anxiety status was assessed among patients, study found that anxiety was prevalent among 88.0% patients and 12.0% patients had no anxiety. Among the patients who had anxiety, 36.0% had moderate anxiety, followed by extreme anxiety (30.0%) and high anxiety (22.0%). In a similar study Wahid and partners (2015) reported that 49.1% patients had moderate anxiety, followed by severe (7.8%), high anxiety (5.0%) and relaxed (38.1%).[7] A study done by Bano and colleagues (2018) demonstrated that majority (83.2%) of patients were anxious, 7.4% extremely anxious and 9.5% were not anxious.[15] Another study performed by Zinke et al. (2018) elucidated that most of the patients (69.6%) had low anxiety while 26.1% and 4.3% patients had moderate and high anxiety, respectively.[10]

During study association between self-assessed dental status and dental anxiety level was evaluated, study showed significant association (P=0.014). Likewise significant association (P=0.005) was found between self-assessed dental treatment needs and dental anxiety level. The findings of a study conducted by Syed and associates (2013) also confirmed a significant association between dental status and dental anxiety level as well as dental treatment needs and dental anxiety level.[23]

CONCLUSION

Study concluded that dental anxiety was prevalent among majority of the patients and it has significant association with self-assessed dental status and dental treatment needs of adult patients. Further studies are needed on vast level to assess the dental anxiety and its association with self-assessed dental status and treatment needs among adult patients.

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BEST POLICY FOR MINIMIZING THE POST OPERATIVE ASCITES IN CHRONIC LIVER DISEASE PATIENTS

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Abstract

Background: Operations in general surgery are being performed in patients with chronic liver disease in emergency or on elective list like appendectomy, cholecystectomy and obstructed hernias. Normal preoperative investigations reveal cirrhotic livers per-operatively in 3-4% patients. These patients can develop or exaggerate post-operative ascites which is sometimes difficult to manage leading to increase in morbidity & mortality. So, we assessed the effect of combination of treatment options in these patients regarding the outcome.

Objectives: The purpose of this study was to find out the best policy to reduce the development of post-operative ascites in chronic liver disease patients when operated for general surgery procedures.

Methodology: This study was conducted at Avicenna Medical & Dental College, Bedian Road, Lahore from January to December 2020. Fifty patients were randomly included in the study and counselled for dietary sodium restriction. Treatment options including infusion of crystalloids or colloids, use of diuretics and need for paracentesis were observed in all patients and outcomes noted.

Results: The patients who received combination of treatment options during their peri-operative period, developed minimum or no ascites. Preoperatively corrected albumin and judiciously used intravenous fluids have important role in reduction of development of postoperative ascites.

Conclusion: Dietary sodium restriction, post-operative infusion of crystalloids or colloids, use of diuretics and paracentesis when required, is a successful approach to reduce the development of post-operative ascites in chronic liver disease patients when they are being operated for general surgery procedures.

Key Words: General surgery procedures, Chronic liver disease, Post-operative, Ascites,

The major complication of cirrhosis is ascites[1] Over the ten years of follow up, it occurs in 50% of patients.[2] In the natural history of cirrhosis, the development of ascites is an important landmark. Over two years it is associated with a 50% mortality,[2,3,4,5] for which liver transplantation is considered as a therapeutic option.[3] The underlying cause of cirrhosis leading to ascites in majority (75%) of patients is malignancy (10%), heart failure (3%), tuberculosis (2%), pancreatitis (1%) and other rare causes as well.[6]

In 1993, mortality from cirrhosis was 6 per 100 000 population and in 2000, it increased to 12.7 per 100 000 population.[7]

10–20% of population has non-alcoholic fatty liver disease, alcoholic liver disease or chronic hepatitis C to develop cirrhosis over a period of 10–20 years. Abnormal liver function is seen in approximately 4% of the general population.[8]

Over the next few years, a huge increase in the burden of liver disease is expected[8] leading to inevitable increase in complications of cirrhosis. Over recent years, several changes have been considered in the clinical management of cirrhotic ascites.

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Reduction of salt intake is the most important step to treat the ascites. Recommended limit is 2 g or less in a day. Because it is difficult to determine the salt content in foods so dietitian involvement is helpful. Salt substitutes free of potassium can be used.[9]

Diuretics are routinely used to treat ascites. Spironolactone or furosemide can cause electrolyte and kidney function imbalance. Diuretics are not substitute for salt restriction. Both are required to manage ascites.

Sometime, despite the use of diuretics and salt restriction, ascites is refractory. In these cases, patients may need paracentesis to remove large amount of excess fluid.

Portosystemic shunt is sometimes used as a treatment when paracentesis is failed. It relieves portal hypertension and diminishing ascites by increasing blood flow to all organs of body. Liver transplant is reserved for patients with very severe cirrhosis with liver failure.[10]

METHODOLOGY

This study was conducted at Avicenna Medical & Dental College, Bedian Road, Lahore from January to December 2020. Fifty patients were randomly included in the study and counselled for dietary sodium restriction. Treatment options including preoperative correction of hypoalbuminemia, postoperative infusion of crystalloids or colloids, use of diuretics and need for paracentesis, were applied in all patients and outcome observed.

RESULTS

The patients who received combination of treatment options during their peri-operative period, developed minimum or no ascites. Preoperatively corrected albumin and judiciously used intravenous fluids have important role in reduction of development of postoperative ascites.

DISCUSSION

A negative sodium balance by dietary salt restriction alone can occur in 10% of patients with chronic liver disease.[11] It is associated with lower diuretic requirement, faster resolution of ascites and shorter hospital stay.[12,13]

In the past, dietary salt restricted to 22 or 50 mmol/day was considered adequate. Protein malnutrition may occur due to this diet pattern[14] and is not recommended now a days. By adopting a no-added salt diet and avoidance of pre-prepared food stuffs, dietary salt can be restricted up to ~90 mmol/day (5.2 g).[15,16]

High sodium content is present in certain drugs, especially effervescent tablets. Intravenous antibiotics usually contain 2.1–3.6 mmol of sodium per gram but injection ciprofloxacin contains 30 mmol sodium in 200 ml (400 mg). In patients with ascites, it is preferable to avoid infusion of fluids which contain salt. In hepatorenal syndrome or renal impairment with severe hyponatremia, volume expansion with crystalloid or colloid is advised.

For resolution of ascites, water restriction has not been proved beneficial but most experts describe no role of water restriction in patients with uncomplicated ascites. In patients with ascites & hyponatremia, normal saline infusion is recommended. Diuretics are mainstay of treatment in ascites since 1940 when its availability was started.

Repeated large volume paracentesis is required for patients with large or refractory ascites. Large volume paracentesis with colloid replacement is rapid, safe and effective according to several controlled clinical trials.[17,18,19,20,21] As compared to diuretic therapy, serial large volume paracentesis (4–6 l/day) with albumin infusion (8 g/liter of ascites can be removed) is more effective with fewer complications & shorter hospital stay.[18]

Many studies also evaluated the efficacy, safety, speed & hemodynamical changes after paracentesis and need for colloid replacement therapy. Total paracentesis is safer than repeated paracentesis generally if volume expansion is being required after the procedure.[8,9] Circulatory dysfunction with renal function impairment and electrolyte imbalance can occur after paracentesis if volume expansion is failed.[21,22,23,24,25]

In majority of patients (93%), ascites recurs

post-paracentesis if diuretic therapy is not restarted[94] Reinstitution of diuretics after paracentesis, usually within 1–2 days does not cause post-paracentesis circulatory dysfunction.

In our study, we observed that the patients with chronic liver disease who developed postoperative ascites, respond well to combination of treatment options including dietary salt restriction, preoperative correction of hypoalbuminemia, judicious use of intravenous fluids and use of diuretics. Paracentesis was needed only in one patient out of fifty (0.02%).

CONCLUSION

Dietary sodium restriction, pre-operative correction of hypoalbuminemia, infusion of crystalloids or colloids in postoperative period, use of diuretics and paracentesis when required, is the best policy to reduce the development of post-operative ascites in chronic liver disease patients when they are being operated for general surgical procedures.

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EFFECT OF HELICOBACTER PYLORI ERADICATION ON PLATELET RECOVERY FOR IDIOPATHIC THROMBOCYTOPENIC PURPURA IN PAKISTANI POPULATION

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Abstract

Background: Helicobacter Pylori (H. pylori) is prevalent in more than 50% population around the globe. Recent advances showed the association of H. Pylori with idiopathic thrombocytopenia (ITP) resulting in low platelet count.

Objective: We aimed to determine the effects of H pylori eradication therapy on platelet count in ITP patients in Pakistan.

Methodology: In this study, a total of 300 patients were enrolled to meet the criteria of ITP. 150 patients each were included in the test and control groups. Test group patients have ITP along with H. Pylori infection whereas in control group, only ITP positive patients were included without H. Pylori infection. An antibiotic treatment regimen was given to test group and the platelet count was checked after 1, 3 and 6 months' intervals in both the groups. The status of infection is also considered in each case after eradication treatment.

Results: Out of 150 H. Pylori positive individuals in test group, 120 (80%) were successfully eradicated after the treatment and the platelet count was significantly increased by the 6th month. A complete response is achieved in 8% cases, whereas, partial response is seen in 23% cases. The 30 individuals (20%) in test group remains H. pylori positive (non-responder) even after eradication treatment and their platelet count was much lower as compared to the H. Pylori negative (eradicated) individuals.

Conclusion: H. Pylori screening for ITP patients in recommended as the positive association between ITP and H. Pylori infection has been found in this study.

Keywords: H. Pylori, ITP, platelets, responder, non-responder, eradication

H pylori is a gram negative spiral shape micro-aerophilic bacterium first isolated by Warren and Marshall in 1984 with a potential to cause peptic ulcers and B type gastritis.[1] More than half of the population is infected with this pathogen both in developed and developing countries[2,3] H. Pylori is transmitted in individuals via fecal-oral, oral-fecal or oral-oral routes.[2,4] The risk factors for the infection include low socioeconomic status, overcrowding, low education rates, poor health conditions and poor sanitation.[4] The association of ITP with H. Pylori and platelet recovery with eradication therapy was first identified by Gasbarrini.[5] Up till now many authors form different countries and geographical areas has documented the effect of eradication therapy but the results came out to be highly variable.[6]

H. Pylori pathogenesis occurs in two steps, the first step involves colonization of host by various factors including urease production that provides

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acidic environment needed for its survival, flagella, motility, ATPase and adhesion. In the second step, the bacterium produces various virulence factors including vacuolating associated cytotoxic gene A (VasA), cytotoxic associated gene A(CagA), lipopolysaccharides, heat shock protein and neutrophil activating protein promoting tissue lesion.[7-9] After colonization in gastric mucosa it causes chronic atrophic gastritis in all colonized patients leading to peptic ulcers, gastric carcinoma and MALT(mucosal- associated lymphoid tissue) lymphoma.[10]

H pylori is also associated with Extra intestinal manifestations including acute myocardial infarction[11] and with systemic disorders like autoimmune thyroiditis and hematological diseases.[12] In hematological diseases, association of unexplained iron deficiency anemia with H pylori is proven.[13] Meta-analysis showed that eradication of H Pylori increases hemoglobin and improve anemia.[14,15]

Idiopathic thrombocytopenic purpura(ITP) is a diagnosis of exclusion, it is labeled by physicians after ruling out all other possible causes of thrombocytopenia.[16] ITP is an autoantibody immune mediated destruction and decreased production of platelet.[17] Gasbarrini et al first time reported H pylori association with ITP[5] Showing that H pylori is more prevalent in ITP patient, but there is no clear evidence predicting that these patients will have more severe thrombocytopenia[18] Several studies have showed the efficacy of H pylori eradication therapy resulting in platelets increase in ITP patients with excellent sustain response during follow up period.[19-24] Role of H pylori eradication in reversibility of ITP is documented in few randomized and non-randomized trial contributing to conflicting data regarding the eradication and sustained response of platelet improvement.[25-27] Response to eradication therapy occur in half of ITP patients, more frequently documented in Japanese and Italian patient.[28] However, many studies done in the past reported no correlation with H pylori eradication therapy with improvement of platelet count in ITP patients.[29-33]

The conflict in data arises due to various factors including the severity of disease, geographical distribution, prevalence and virulence factors of H pylori. ITP is common in Pakistani region and many patients are diagnosed with ITP with proper explanation. The aim of this study is to see the effect of H pylori eradication therapy on reversibility of low platelets in ITP patients during follow up period in province of Punjab Pakistan. In 2009, a similar study was conducted by shaikh et al in Pakistan which is the only study conducted in this region.[34] However, the study does not document the effects of eradication therapy as the potential treatment for ITP. In our study, we indicate the statistics along with treatment outcome with the aim of proposing eradication therapy against ITP in Pakistan.

METHODOLOGY

Single center sequential observational study was conducted in Lahore General Hospital, Lahore. All patients provided written informed consent before enrollment. The study was approved by ethical committee board of Institution, Lahore General Hospital. Patients between 16 to 70 years were eligible if they had platelet count more than 30000 and less than 100000 (/uL). Major inclusion criteria included the current H pylori infection. Exclusion criteria included previous treatment of H pylori, cirrhosis, hematological malignancy, chronic hepatitis B and C, prolong use of medicinal steroids, and any known cause of thrombocytopenia.

H pylori infection was confirmed by stool antigen, serology tests and Wright Gimsa stain sample taken by endoscopy from greater curvature and other standard area. Before starting the treatment, platelet counts of all patients were checked. H pylori eradication therapy includes sequential therapy of amoxicillin 1g, Tinidazole 500mg and Omeprazole 20mg twice a day for first five days and next five days with levofloxacin 500mg, azithromycin 500mg and omeprazole 20mg twice a day.

Treatment response was checked after one-month interval for H pylori eradication by stool antigen and Histopathology tests of upper GI tract. On the basis

of treatment response, the participants were divided into three groups, H pylori positive and eradicated group, H pylori positive-non eradicated group (non-responders) and H pylori negative group (control group). Platelet count were checked regularly after one month, three months and six months of treatment.

All categorical variables were described as frequency and continuous range mean and standard deviation. As per definition platelets more than 100 defined as responder and platelets count double than baseline after H pylori eradication but less than 100 partial responders and other than this non responders or failed to give any response. Mean of all 3 values compared by ANOVA and p valued measured by Mann Whitney u test. All data analyzed on SPSS version 22.

RESULTS

We defined complete response if platelets increased more than 100,000, partial response if platelets doubles or increase 30000 from baseline count and failure if platelet count is not increased more than double of base line count. Out of the 150 H. Pylori Positive thrombocytopenic patients (test group), 120 (80%) were successfully eradicated with no reported relapse whereas 30 (20%) patients were non-responders (fig. 1). The study cohort along with main outcomes is summarized in figure 2. Out of the 30 non-responder individuals, 18 (60%) were previously treated whereas in the responders group, only 6.6% were previously given treatment.

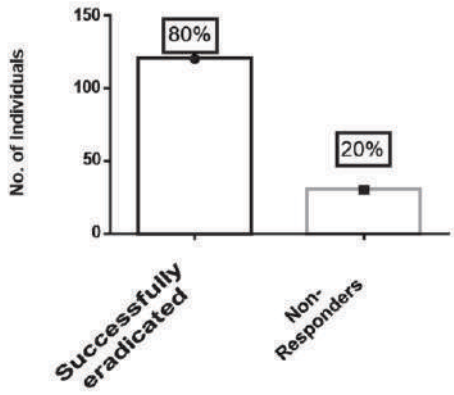

Figure 1: *Responders and non-Responders Individuals to the Eradication Therapy after 6 Months' Antibiotics Regime*

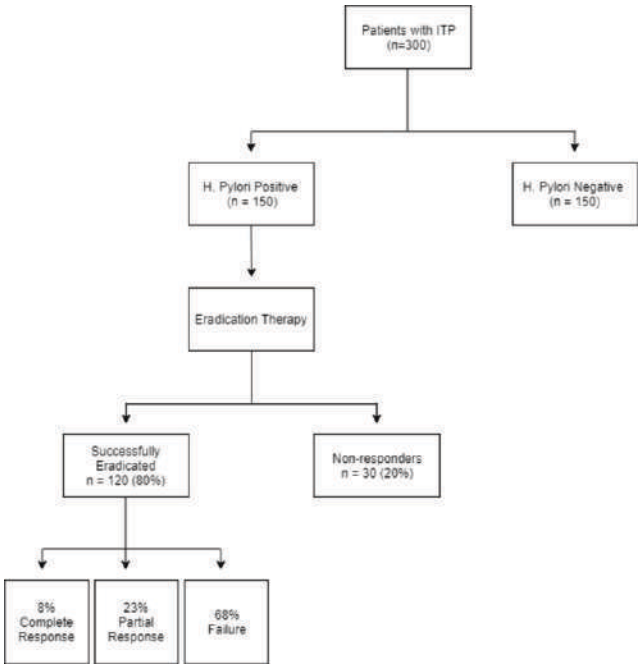

Figure 2: *Study Cohort Analyzing 300 Patients with for Idiopathic Thrombocytopenic Purpura and H. Pylori Infection from Lahore, Pakistan, 2018*

On analysis of successfully eradicated patients, differential results are obtained. On the basis of criteria described above, 10 out of 120 (8%) showed complete response with the platelet increase of more than 100000 after eradication therapy. Partial response is shown by 28 out of 120 H. Pylori positive-eradicated individuals (23%) with the increase of more than double from the base line. 82 individuals (68%) failed to increase the platelet count more than double after eradication therapy from base line, however, a slight increase in platelet count from baseline values is still evident in these 56 patients (fig 3). Gender distribution pattern showed the high ratio of prevalence in females i.e. 53.3 whereas in males, ratio comes out to be 46.6% (Table 1) (fig 4).

The responders were successfully eradicated after 6 months of the therapy with the response rate of 46.6% in males and 53.3% in females. The gender distribution of the study participants indicates the higher prevalence ratio in females (64/120 F in responders and18/30 F in non- responders). No relapse was reported in either gender on follow up. Out of 30 non responders 40% were males whereas 60% were

females (table 1).

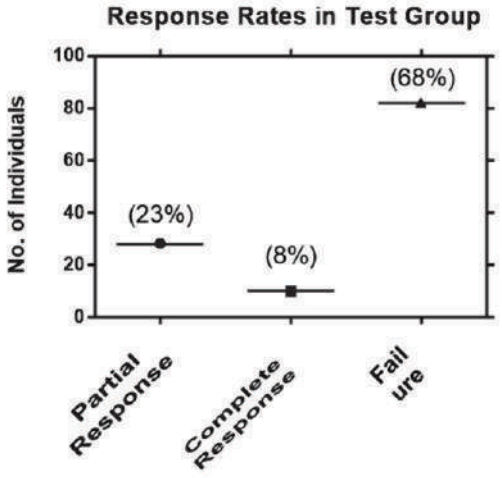

Figure 3: *Population Percentage showing Partial Response, Complete response and Failure in Platelet Recovery after Eradication Therapy*

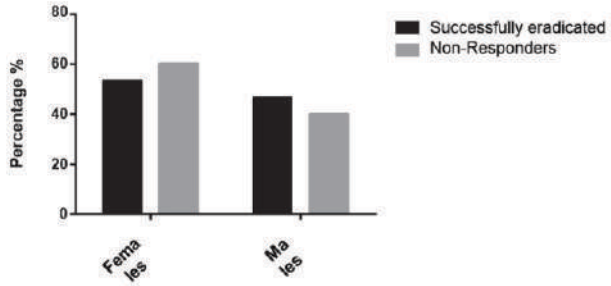

Figure 4: *Treatment Efficacy Along with Gender Distribution of Study Participants*

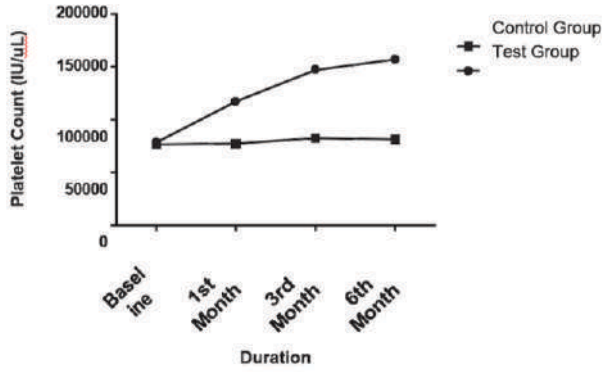

Figure 5: *Mean Platelet Count in Test Group (Patients with ITP and H. Pylori Along with Eradication therapy) VS Control Group (Patients only with ITP with no Treatment Given)*

The platelet counts in test and control group do not differ significantly at baseline level (78000 IU/uL vs 76000 IU/uL). However, on average, the platelet count increase sharply in H. Pylori eradicated group as compared to non-eradicated group showing an association between ITP and H Pylori infection. The statistical analysis showed the mean platelet count in responder group to be higher as compared to non-responders (64.16±17.49 vs 59±15.55) with the P-value of 0.45 (table 1). The control group having only ITP and no treatment do not show any increase in their platelet count. (Fig 5). Statistical analysis showed the mean platelet count in responder group to be higher as compared to non-responders (64.16±17.49 vs 59± 15.55) with the P-value of 0.45. (Table 1).

Table 1: *Comprehensive Account of the Patient's Demographics and Clinic Parameters in Successfully Eradicated Patients*

Demographics	Responders	Non-Responders	P-Value
Males	56 (46.6%)	12 (40%)	0.08
Females	64 (53.3%)	18 (60%)	0.06
Mean Age (Male)	40±14.18	36±18.26	0.43
Mean Age (Female)	35±12.24	34±13.11	0.78
Previously Treated	8 (6.6%)	18 (60%)	
Platelet count at baseline $-\times10^9$/L	64.16±17.49	59±15.55	0.45

Data are presented as number percentages and means ± (standard deviation). The p-values were calculated using the Statistical Package for the Social Sciences (SPSS) for Windows (SPSS Inc., Chicago, Illinois).

DISCUSSION

H. Pylori is considered as the infectious agent with the ability to cause gastritis, gastric cancer, peptic ulcer and lymphoid tissue lymphomas.[35] The immunologic response against the H. Pylori pathogen determines the gastric mucosal injury by releasing the cytokines along with the action of antibodies.[36]

ITP is an auto-immune disorder mediated by the anti-platelets anti-bodies (Abs). These Abs bind to the platelets and magekaryocytes to bring about the accelerated destruction of platelets by reticuloendothelial system.[37] Till date the causative factors of ITP are obscure but a particular subset of ITP is known to

be associated with viral or bacterial infections, indicating the involvement of infection pathogenesis in the onset of ITP.

Recently the association is found between Idiopathic thrombocytopenic purpura and H. Pylori based on the observation that platelet count increases in the individuals that have undergone eradication therapy against H. pylori.[38,39] However, H. Pylori prevalence is similar in general population as well as in the ITP patients, indicating that the association between the two could be incidental.[19] This arises the question that how H. Pylori treatment by eradication therapy increases platelet count and the most possible explanation is that H. Pylori eradication has a therapeutic effect.[40] Another explanation on how H. Pylori contribute to ITP development is given by Gerhard et al., is the production of Lewis (Le) antigens by H. Pylori in strain specific manner. These antigens bind to platelets and acts as targets against anti-Le antibodies.[41] literature indicated that the response rates of eradication therapy differs greatly in different geographical regions.[6]

In this study, a comprehensive research on 300 individuals has been conducted with the main aim of establishing the platelet recovery pattern and eradication therapy response in Pakistan. Out of 150 H. Pylori positive ITP patients, 120 showed the positive response, giving eradication rate of 80%, which is compatible with the other study results showing and eradication rate of more than 75%,[34,42] whereas, the remaining 30 out of 120 were non-responders.

The platelet count haven been demonstrated in the 120 eradicated patients. The complete response of platelet recovery is shown in only 8% individuals, whereas partial recovery response is evident in 23% participants. These results are in accordance with the studies carried out in US[39] and Italy.[43] The demographics part of this study showed that the higher incidence of ITP is found in females with the mean age of ±54 in both the genders.[39]

In contrast to our results, some studies showed that eradication therapy imparts no favorable effects on ITP patients. A study conducted in Italy reported no increase in platelet count after the therapy.[29] Another study conducted in US and UK demonstrated poor response of ITP patients against ITP therapy.[44,45] However, some other studies indicated successful treatment of ITP by eradication therapy. These results showed the diversity of treatment outcomes and possible involvement of geographical regions in determining the treatment efficacy against ITP. Gender distribution pattern in our study is also in accordance with other studies showing a high prevalence rates in females.[23,42]

CONCLUSION

These results indicated the stronger association of H. Pylori with ITP patients as compared to the general population and the eradication therapy mainly consisting of antibiotics can help in increasing the platelet count. But the therapy and its response is effective to only a limited extent. However, H. Pylori screening in ITP patients is recommended and further studies are needed to testify the association between IPT and H. Pylori infection.

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THE EFFECT OF VARICOCELECTOMY ON SPERM PARAMETERS IN INFERTILE MEN WITH VARICOCELE HAVING NORMAL SPERM COUNT BUT DECREASED MOTILITY AND MORPHOLOGY

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Abstract

Background:. To compare preoperative and postoperative sperm parameters such as sperm count, motility, and morphology in patients with normal sperm concentration with teratozoospermia and asthenozoospermia.

Methodology: One hundred and six patients with varicocele associated with male infertility over a 5-year period were included into the study. Pre- and postvaricocelectomy seminal fluid parameters evaluation according to the World Health Organization (WHO) criteria was performed at 4–6-month intervals.

Results: One hundred and six patients met the criteria. The mean age of patients was 24.53 ± 8.13. The mean duration of infertility was 3.6 years (range: 1.5–6.3). Only the sperm motility of patients presenting with normospermia showed a significant improvement postoperatively.

Conclusions: No significant improvement in sperm morphology may be obtained in patients with clinical varicocele and preoperative normospermia.

Key Words: Varicocele, sperm count, infertile men

Infertility has evolved as one of the world's major public health problem, affecting one of every six couples trying to conceive.[1,2] The incidence of infertility is 10–15% among couples trying to conceive, with male infertility contributing to nearly 50% of cases.[3] Although multiple factors may play a role in male infertility, varicocele is the most frequent finding in male infertility, with a prevalence of 19–41% of men with primary infertility and 45–81% of men with secondary infertility.[4] Increased scrotal temperature, reflux of metabolites from the kidney and adrenal gland, decreased volume of blood flow, and anoxia are the supposed mechanisms.[5] Varicocele is also known as the most surgically correctable cause of male infertility, and its repair is the most commonly performed surgical procedure in order to correct male infertility.[6] Previous studies have shown abnormalities in the sperm count, motility, and morphology in varicocele patients and a significant improvement in these parameters following surgical correction.[7] The postoperative outcomes of varicocelectomy operation in patients with normal sperm count but with sperm having abnormal morphology and impaired motility have not been studied much. Therefore, in this retrospective study, we compared preoperative and postoperative sperm parameters such as sperm count, motility, and morphology in patients with normal sperm concentration showing abnormal forms and decreased motility pattern.

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METHODOLOGY

The study included 106 patients seeking surgical treatment for varicocele in our institution from May

2016 to October 2020. There were no documented diseases that would affect the results. A basic infertility evaluation including a detailed history and a thorough physical examination was carried out. All of the patients were married with primary infertility and varicocele (grade 1–3) having normospermia either having sperms with decreased normal forms and/or motility (progressive motility and nonprogressive motility). All the patients with varicocele were tested by way of color Doppler ultrasound which identified it as anechoic tubular structures that dilated on Valsalva maneuver. Volume, pH, sperm density, morphology, and motility were evaluated. The normal semen parameters according to the WHO Manual for Semen Analysis were as follows:[7] volume of semen in adult males: 1.5 mL, sperm concentration: >15 million, sperm morphology (normal forms): 4%, progressive and nonprogressive motility (PR+NP): 40%, and progressive (PR): 32%. supra –inguinal(high ligation) varicocelectomy was performed for all of the patients by a single urologist. Four weeks after the operation, a Doppler ultrasonography imaging was performed to confirm the improvement of varicocele by the absence of venous back flow. We followed up the patients for 3 and 6 months, and seminal analysis was performed to evaluate changes in the seminal indices.

The data was analyzed using the SPSS 14.0 statistical software for Windows. For independent variables, we used independent sample t-test, and for dependent variables, paired sample t-test was utilized. Values less than 0.05 were considered statistically significant.

RESULTS

One hundred and six patients met the criteria set for this study. The mean age of patients was 28.6 at commencement of the study. The mean duration of infertility was 3.6 years (range: 1.5–6.3). The pair wise comparison of the preoperative and the postoperative sperm concentrations in all the normospermic patients did not show any significant improvements (P=0.105) after varicocelectomy (Table 1). Asthenozoospermia defined as sperm consisting of poor forward motility and represented as PR+NP motile sperms was found in 92 (87%) patients preoperatively. Postoperatively, asthenospermia was found in 42 (40%) of the patients. When the sperm motility of the patients obtained postoperatively was compared with the preoperative values using a paired t-test, there was a significant improvement in the sperm motility overall (P=0.000) (Table 1). Teratospermia was defined as normal sperm morphology of less than 4%. Forty-nine (46%) patients were found to have teratozoospermia preoperatively. Following varicocelectomy, teratospermia was seen in 40 (38%) patients. Paired comparison of the preoperative and postoperative semen analyses showed that there was no significant improvement in sperm morphology after varicocelectomy in the overall group (Table 1).

Table 1: *Effect of varicocelectomy on Semen Parameters in Patients with Normal Sperm Density (>15 million/mL).*

No. 106	Sperm count	Morpho-logy %	Motility (a) %	Motility (a+b) %
Preoperative	59.9±40.2	3.6±1.6	15.4±8.0	29.7±10.7
Postoperative	60.4±43.2	3.7±1.4	20.4±8.4	40.3±10.7
P value	0.105	0.400	0.000	0.000

DISCUSSION

Testicular varicose veins cause reduction in function and number of the testicular cells which is reflected as an altered sperm parameter.[8] Surgical treatment is indicated in men with varicocele when the semen analysis shows oligospermia, asthenospermia, teratospermia, or coexistence of these abnormalities. To date, previous studies have demonstrated a beneficial effect of varicocelectomy in subfertile men with varicocele who have poor sperm quality.[9] It is also known that several patients with clinical varicoceles have isolated abnormalities such as sperm motility or morphological parameters in the semen analysis, and varicocelectomy is carried out in these patients as well. However, adequate studies have not been presented in regards to varicocelectomy being beneficial in such patients. In this study, we tried to examine the changes in the semen parameters after varicocelectomy among the patients who have normal sperm

count associated with asthenospermia and/or teratospermia.

Evidence suggests that men with normospermic varicocele respond to varicocelectomy differently from those patients who have oligospermia preoperatively due to a different pathophysiological mechanism.[10] Two important studies evaluated the postoperative outcomes of varicocele correction in normospermic patients. In one, isolated teratospermia did not show any significant improvement following varicocelectomy; in the other, neither asthenospermia nor teratozoospermia showed improvement.[9,11] Additionally, authors claimed that performing varicocelectomy exposes this group of patients to the risk of oligozoospermia. Our data also demonstrated that these patients with preoperative normospermia did not show significant improvement in teratozoospermia; the only benefit of surgery was attained towards sperm motility.

The possible explanation is that the poor morphology observed in varicocele patients with normal sperm density may not be only due to the presence of varicoceles. Varicocelectomy in these patients may lead to an unknown alteration or damage to the semen physiology and subsequently morphological abnormalities. With the evidence of the present and previous studies, it may therefore be recommended that normospermic subfertile men with clinical varicoceles and poor sperm motility or morphology should undergo assisted reproductive techniques rather than surgical varicocele ligation.

There are also limitations to our study; first, it is a retrospective study; second, there is lack of data concerning outcome of pregnancy and conceptions.

In conclusion, normospermic subfertile men with clinical varicoceles and teratozoospermia may not show statistically significant improvement in sperm morphology following varicocelectomy. We think that varicocelectomy as a choice for normospermic patients with teratospermia should be carefully considered. Comprehensive multi-institutional studies are necessary to confirm the present findings and would vastly benefit doctors and patients in the future.

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DIAGNOSTIC ACCURACY OF DOPPLER ULTRASONOGRAPHY IN ANTENATAL DETECTION OF MORBIDLY ADHERENT PLACENTA IN PATIENTS WITH HISTORY OF PREVIOUS UTERINE SURGERY, TAKING OPERATIVE FINDINGS AS GOLD STANDARD

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Abstract

Background: The diagnosis of morbidly adherent placenta is usually made based on clinical history, imaging findings, and histological features. When abdominal ultrasonography cannot definitively exclude morbidly adherent placenta as a diagnosis, the next imaging technique used is Doppler ultrasonography. In high-risk patients, magnetic resonance imaging (MRI) is the gold standard in antenatal diagnosis, although it is not as widely available as (and therefore more expensive than) ultrasonography.

Objectives: To determine the diagnostic accuracy of Doppler ultrasonography in antenatal detection of morbidly adherent placenta in patients with H/O previous uterine surgery, taking operative findings as gold standard.

Methodology: A total of 148 pregnant women with singleton pregnancy of gestational age >37 weeks of age 18-40 years were included. Primigravida were excluded. After taking informed consent, ultrasound was done on Toshiba Xario 200 Doppler ultrasound machine using 3.5 MHZ curvilinear transducer. Each Doppler USG findings were interpreted by one consultant radiologist and were looked for presence or absence of morbidly adherent placenta. All patients were then undergone surgery in the concerned ward and operative findings were noted for morbidly adherent placenta. Doppler USG findings were compared with operative findings.

Results: In Doppler USG positive patients, 76 true positive while 05 were false positive. Among, 67 doppler USG negative patients, 07 were false negative while 60 were true negative. Overall sensitivity, specificity, positive & negative predictive value & diagnostic accuracy of Doppler ultrasonography in diagnosing morbidly adherent placenta in patients with previous uterine surgery, taking operative findings as gold standard was 91.57%, 92.31%, 93.83%, 89.55% and 91.89% respectively.

Conclusion: This study concluded that Doppler ultrasonography is a highly sensitive and accurate modality for diagnosing morbidly adherent placenta, and has not dramatically improved our ability of diagnosing morbidly adherent placenta but also improves patient care by accurate diagnosis.

Key Words: morbidly adherent placenta, Doppler ultrasonography, sensitivity.

Morbidly adherent placenta is a major cause of maternal morbidity & mortality and now the common reason for emergency postpartum hysterectomy. It is an abnormal attachment of the placenta to the myometrium, & occurs when a defect of the decidua basalis allows the chorionic villi to invade the myometrium.[1] The depth of myometrial invasion is used to classify placenta accreta. Villi partly invade the myometrium in placenta increta. Placenta percreta is the severe type, in which villi reach the entire myometrial thickness or beyond the serosa.[2,3]

A pathologic specimen collected during hysterectomy is used to diagnose placenta accreta. This definitive diagnosis is dependent on the visualization of chorionic villi embedded in the myometrium with absence of the decidual layer between them.[4,5] Con-

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ventional 2-dimensional sonography has been shown to be a best screening method for the detection of placenta accreta. Patients that have had a previous cesarean delivery and have a placenta previa are usually screened for accreta using antenatal sonography, but the diagnosis is made postpartum by pathologic demonstration of chorionic villi invading the myometrium & absence of decidua.[6]

Medical history, imaging observations, and histological features are commonly used to make the diagnosis of a morbidly adherent placenta.[6,7] Magnetic resonance imaging (MRI) in high-risk patients is a gold standard in antenatal diagnosis, but not as available (and is also more expensive than) ultrasonography.[8] In a study,[9] prevalence of morbidly adherent placenta was found in 21% women and sensitivity and specificity of Doppler ultrasonography in diagnosing morbidly adherent placenta as 87% and 63% respectively. In another study,[10] sensitivity & specificity of Doppler ultrasonography in diagnosing morbidly adherent placenta was found to be 90.70% and 96.90% respectively. One more study published by Lim et al[11] reported that Doppler sonography had a 67% sensitivity and 50% specificity.

While many studies are available on this but as described above, the studies have shown different results in this regard, so there must be reassessment of the data. Keeping in mind all this, I have decided to conduct this study to determine the diagnostic accuracy of Doppler ultrasonography in diagnosing morbidly adherent placenta in patients with previous cesarean section, taking operative findings as gold standard. The results of my study will be a useful addition in the existing literature and if it's diagnostic accuracy will be found high, then we can provide these particular patients with a non-invasive imaging modality which can be used routinely in our general practice for prenatal diagnosis of this condition and allow prompt and timely management, thus imparting a major influence at national level in reducing both maternal and fetal mortality and morbidity due to this devastating complication.

METHODOLOGY

This descriptive cross sectional study was conducted from 7th July 2018 to 6th January 2019 in the Radiology department of Sharif Medical City, Lahore. It was after obtaining permission from the Institutional Board of the hospital. Informed written consent was obtained from patients. Sample size of 148 cases has been calculated with 95% confidence level, and taking prevalence of placenta accreta as 21% and desired precision 10% for sensitivity of 87% and specificity of 63% of Doppler ultrasonography in diagnosing morbidly adherent placenta.[9]

All pregnant women presenting with 18-40 years of age and also with singleton pregnancy (assessed on ultrasonography) of gestational age >37 weeks (assessed on LMP) and previous uterine surgery or Gravidity1-5 were included from the study. Patients with primigravida and not willing to participate in the research were excluded from the study.

After taking informed consent, ultrasound was done on Toshiba Nemio XG (SSA-580A) Doppler ultrasound machine using 3.5 MHZ curvilinear transducer. Each Doppler USG findings were interpreted by one consultant radiologist (at least 3 years of post fellowship experience) and were looked for absence or presence of morbidly adherent placenta.

All patients were then undergone surgery in the concerned ward and operative findings were noted for morbidly adherent placenta (as described in operational definition). Doppler USG findings were compared with operative findings. All this data including the demographic data (age, BMI, gestational age, gravidity, number of previous c/sections, place of living and placenta accreta on Doppler USG and operative findings) was recorded on a specially designed proforma

Data was entered in SPSS 20. Age, duration of age, gestational age, gravidity, BMI and number of previous surgeries presented ad mean and standard deviation. Categorical data like place of living (rural/urban) and morbidly adherent placenta on Doppler USG and operative findings (present or absent) were presented as percentage & frequencies. 2×2 contingency table was used to calculate sensitivity, specificity,

positive predictive value, negative predictive value & diagnostic accuracy of Doppler ultrasonography in diagnosing morbidly adherent placenta in patients with previous uterine surgery, taking operational findings as gold standard. Effect modifiers like age, gestational age, and gravidity, number of previous uterine surgeries, BMI and place of living (rural/urban) were controlled by stratification. Post-stratification chi square will be applied and p-value ≤ 0.05 was taken as significant. Diagnostic accuracy was also calculated.

RESULTS

In our study, total 148 patients were included, the mean age was 28.82 ± 3.80 years. Most of the patients 115 (77.70%) were between 18 to 30 years of age as shown in Table I.

The average gestational age was 38.61 ± 1.22 weeks. Average gravidity was 2.23 ± 0.64. Mean number of previous uterine surgeries were 1.24 ± 0.64. Mean BMI was 28.66±2.80 kg/m^2. Table: 1 Distribution of patients according to place of living is shown in Table: 2

All the patients were subjected to Doppler USG. Doppler USG showed the morbidly adherent placentain 81(54.73%) patients. Operative findings confirmed morbidly adherent placentain 83(56.08%) cases where as 65(43.92%) patients' revealed no morbidly adherent placenta. In Doppler USG positive patients, 76 were true positive while 05 were false positive. Among, 67 doppler USG negative patients, 07 were false negative while 60 were true negative as shown in Table: 3

Overall sensitivity, specificity, positive & negative predictive value and diagnostic accuracy of Doppler ultrasonography in diagnosing morbidly adherent placenta in patients with previous uterine surgery, taking operative findings as gold standard was 91.57%, 92.31%, 93.83%, 89.55% and 91.89% respectively. Table: 3 Stratification of diagnostic accuracy with respect to age group, Gestational age stratification, gravidity, number of previous uterine surgeries, BMI and place of living is shown in Table 4,5,6,7,8,& 9

DISCUSSION

The introduction of obstetric ultrasound with color Doppler in modern obstetrics helped in the early detection & management of adherent placenta. With such success, these low-cost modalities may be able to fully replace MRI in the diagnosis of morbidly adherent placentas. While statistically a rare complication, placenta accrete has now become an important etiology of maternal morbidity & mortality.[12] Owing to the increasing rate of Cesarean delivery, there has been a

Table 1: *Distribution of Patients According to Age, Gestational age, Gravidity and BMI*

		Frequency (%)
Age	**Mean± SD**	28.82±3.80
	18-30	115(77.70%)
	31-40	33(22.30%)
Gestational Age	**Mean± SD**	38.61±1.22
	37-39	108(72.97%)
	40-41	40(27.03%)
Gravidity	**Mean± SD**	2.23±0.64
	≤ 2	97(65.54%)
	≥ 2	51(34.46%)
BMI (kg/m^2)	**Mean± SD**	
	≤ 27	61(41.22%)
	>27	87(68/78%)

Table 2: *Distribution of Patients according to Number of Previous Uterinr Surgeris and Place of Living*

		Frequency (%)
Previous uterine surgeries	**< 2**	96(64.86%)
	≥ 2	52(35.14%)
Place of living	**Rural**	66(44.59%)
	Urban	82(55.41%)

Table 3: *Diagnostic Accuracy of Doppler Ultrasonography in Diagnosing Morbidly Adherent Placenta1in Patients with Previous Uterine Surgery, taking Operative Findings as Gold Standard.*

	Positive result on surgery	**Negative result on surgery**
Positive result on Doppler USG	76(TP)	05(FP)
Negative result on	07(FN)	60(TN)
P value	0.0001	
Sensitivity	91.57%	
Specificity	92.31%	
Positive Predictive Value	93.83%	
Negative Predictive Value	89.55%	
Diagnostic Accuracy	91.89%	

*-TP=True positive **Doppler USG-FP=False positive
-FN=False negative *-TN=True negative

Table 4: *Stratification of Diagnostic Accuracy with Respect to Age*

	Age			
	18-30 years(n=115)		31-40 years (n=33)	
	Positive result on Surgery	Negative result on surgery	Positive result on Surgery	Negative result on surgery
Positive Result on Doppler USG	56(TP)	3(FP)	20(TP)	2(FP)
Negative Result Doppler SG	07(FN)	49(TN)	00(FN)	11(TN)
P value	0.001		0.001	
Sensitivity	88.89%		100%	
Specificity	94.23%		84.62%	
Positive Predictive Value	94.92%		90.91%	
Negative Predictive Value	87.50%		100%	
Diagnostic Accuracy	91.30%		93.94%	

Table 5: *Stratification of Diagnostic Accuracy with Respect to Gravidity*

	Gravidity			
	>2 (n=51)		≤2 (n=96)	
	Positive result on Surgery	Negative result on surgery	Positive result on Surgery	Negative result on surgery
Positive Result on Doppler USG	29(TP)	0(FP)	47(TP)	05(FP)
Negative Result Doppler USG	04(FN)	18(TN)	03(FN)	42(TN)
P value	0.001		0.001	
Sensitivity	87.88%		94.0%	
Specificity	100%		89.36%	
Positive Predictive Value	100%		90.38%	
Negative Predictive Value	82.82%		93.33%	
Diagnostic Accuracy	92.16%		91.75%	

Table 6: *Stratification of Diagnostic Accuracy with Respect to Gestational Age*

	Gestational Age			
	37-39 weeks (n=108)		40-41 weeks (n=40)	
	Positive result on Surgery	Negative result on surgery	Positive result on Surgery	Negative result on surgery
Positive Result on Doppler USG	58(TP)	03(FP)	18(TP)	2(FP)
Negative Result Doppler USG	04(FN)	43(TN)	03(FN)	17(TN)
P value	0.001		0.001	
Sensitivity	93.55%		85.71%	
Specificity	93.48%		89.47%	
Positive Predictive Value	95.08%		90.0%	
Negative Predictive Value	91.49%		85.0%	
Diagnostic Accuracy	93.52%		87.50%	

Table 7: *Stratification of Diagnostic Accuracy with Respect to Number of Previous Uterine Surgeries*

	Number of previous uterine surgeries			
	<2 (n=96)		≥2 (n=52)	
	Positive result on Surgery	Negative result on surgery	Positive result on Surgery	Negative result on surgery
Positive Result on Doppler USG	51(TP)	03(FP)	25(TP)	2(FP)
Negative Result Doppler USG	01(FN)	41(TN)	06(FN)	19(TN)
P value	0.001		0.001	
Sensitivity	98.08%		80.65%	
Specificity	93.18%		90.48%	
Positive Predictive Value	94.44%		92.59%	
Negative Predictive Value	97.62%		76.0%	
Diagnostic Accuracy	95.83%		84.62%	

10-fold rise in the incidence of placenta accreta since the 1970s.[13]

Color Doppler ultrasound diagnostic accuracy in antenatal diagnosis of MAP in gravid females with placenta previa was calculated as 87.50%, 98.35%, 87.51%, 98.35% & 97.11% as sensitivity, specificity, positive & negative predictive value and accuracy rate respectively.[14] The Doppler ultrasound sensitivity is variable & ranges from 85 to 100% and its specificity from 35 to 96%, depending on the study.[10,15]

Several reports have suggested that neither color Doppler nor power Doppler can assess uteroplacental vascularization or add any additional information to gray-scale ultrasound imaging in the diagnosis of placenta accreta.[16] Despite recent advancement in imaging techniques, no single diagnostic technique affords complete assurance for the presence or absence of placental accreta.[17]

I have conducted this study to determine the diagnostic accuracy of Doppler ultrasonography in

Table 8: *Stratification of Diagnostic Accuracy with Respect to BMI kg/m²*

	Number of previous uterine surgeries			
	BMI ⩽27 kg/m² (n=61)		≥27 (n=87)	
	Positive result on Surgery	Negative result on surgery	Positive result on Surgery	Negative result on surgery
Positive Result on Doppler USG	27(TP)	02(FP)	49(TP)	3(FP)
Negative Result Doppler USG	02(FN)	30(TN)	05(FN)	30(TN)
P value	0.001		0.001	
Sensitivity	93.10%		90.74%	
Specificity	93.75%		90.91%	
Positive Predictive Value	93.10%		94.23%	
Negative Predictive Value	93.75%		85.71%	
Diagnostic Accuracy	93.44%		90.80%	

Table 9: *Stratification of Diagnostic Accuracy with Respect to Place of Living*

	Place of Living			
	Rural (n=61)		Urban(n=87)	
	Positive result on Surgery	Negative result on surgery	Positive result on Surgery	Negative result on surgery
Positive Result on Doppler USG	33(TP)	04(FP)	43(TP)	01(FP)
Negative Result Doppler USG	07(FN)	22(TN)	00(FN)	38(TN)
P value	0.001		0.001	
Sensitivity	82.50%		100%	
Specificity	84.62%		97.44%	
Positive Predictive Value	89.19%		97.73%	
Negative Predictive Value	75.86%		100%	
Diagnostic Accuracy	83.33%		98.78%	

diagnosing morbidly adherent placenta in patients with previous uterine surgery, taking operative findings as gold standard. All the patients were subjected to Doppler USG. In Doppler USG positive patients, 76.0 were true positive while 5 were false positive. Among, 67 doppler USG negative patients, 7 were false negative while 60 were true negative. Sensitivity, specificity, positive & negative predictive value and diagnostic accuracy of Doppler ultrasonography in diagnosing morbidly adherent placenta in patients with previous uterine surgery, taking operative findings as gold standard was 91.57%, 92.31%, 93.83%, 89.55% and 91.89% respectively. Most of the studies compare with our results as shown below

In one study,[10] sensitivity & specificity of Doppler ultrasonography in diagnosing morbidly adherent placenta was found to be 90.70% and 96.90% respectively. In a study,[9] prevalence of morbidly adherent placenta was found in 21% women, sensitivity & specificity of Doppler ultrasonography in diagnosing morbidly adherent placenta as 87% and 63% respectively. Another study published by Lim et al[(11)] reported that Dopplervsonography had a sensitivity of 67% & specificity of 50%.

In a descriptive-analytical study,[18] 150 singleton pregnant women with gestational age of ≥24 weeks with a history of uterine incision (C/S, myomectomy, or metroplasty), underwent a Doppler ultrasonography to detect the position of placenta and evidence for adherent placenta. The Doppler ultrasonography had a sensitivity of 91.66%, a specificity of 100.0%, a positive predictive value of 100.0%, & a negative predictive value of 99.27% in the diagnosis of morbidly adherent placenta.

In a recent study, Budorick et al.[19] reported sensitivity, specificity, PPV, and NPV for loss of myometrial mantle of 79.0%, 77.0%, 61.0% & 89.0%, respectively, for better intraplacental vascularity of 50.0%, 74.0%, 47.0%, and 77.0% respectively, for thrombosed placental lacunae of 43.0%, 77.0%, 46.0%, and 75.0%, respectively, and for loss of bladder wall echogenicity of 21.0%, 100.0%, 100.0%, and 74.0%, respectively. In 2000, Twickler et al found that a smallest myometrial thickness <1 mm identified in third-trimester pregnancies at risk for placental invasion was 100% sensitive and 72.0% specific with a PPV and NPV of 72.0% and 100.0%, respectively.[20]

Dwyer et al.[(21)] studied 32 women to compare the accuracy of trans-abdominal ultrasound & MRI for the diagnosis of placenta accrete. Meng et al[22] presented that 83% ultrasound's sensitivity, its specificity was 95% & diagnostic odds ratio (DOR) was 63.41 compared to 82%, 88% and 22.9% respectively, for MRI. D'Antonio et al[10] published meta analyses for diag-

nosis of invasive placentation with sensitivity of 90.7% & specificity of 96.90% for ultrasound and sensitivity of 94.40% and specificity of 84.0% for MRI.

One more study conducted in southern Saudi Arabia by Maher et al[23] showed that ultrasonography accurately predicted placenta accreta in 33 of 39 of women. They reported sensitivity 95.1% and specificity 95.5%.Pilloni et al[24] in a study using Doppler USG, diagnosed 30/37 women with placental attachment disorder (PAD) due to abnormal invasion, providing a sensitivity of 81.1%, a specificity of 98.9% (274/ 277) and PPV and NPV of 90.9% and 97.5%, respectively.

CONCLUSION

This study concluded that Doppler ultrasonography is a highly sensitive and accurate modality for diagnosing morbidly adherent placenta, and has not only dramatically improved our ability of diagnosing morbidly adherent placenta but also improves patient care by accurate diagnosis and to take proper pre-operative management protocols for placenta accreta. As a result of its non-invasive and high sensitivity, we recommend it as a primary screening method for accurate detection of morbidly adherent placenta in all of these patients in order to minimize maternal morbidity and mortality.

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POSITIVE PREDICTIVE VALUE OF HRCT IN DIAGNOSING PCR NEGATIVE BUT WITH HIGH PRE-TEST PROBABILITY OF COVID-19 PATIENTS

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Abstract

Background: In this time of peak of COVID-19 and high turnover of patients, clinical research is being done enthusiastically to find out new ways not only to improve the diagnosis but also effectively manage the patients. In this scenario, radiological assessment might have a very important role to play which might be a diagnostic priority along with Reverse Transcriptase Polymerase Chain reaction (RT-PCR) in future.

Objective: To determine the positive predictive value of high resolution computed tomography (HRCT) in the diagnosis of COVID-19 patients which have negative PCR results but high clinical suspicion taking antibody titre as gold standard.

Methodology: Retrospective study was conducted over 150 patients within a period of six months i.e., from September 2020 to February 2021. Age group was 18-80 years fulfilling the inclusion criteria. Their HRCT were extracted from the system done on Philiphs. Their antibody titre was noted from their files which was used as gold standard. Statistical analysis was done on SPSS version 20. Sensitivity, specificity, PPV, NPV, diagnostic accuracy and diagnostic odds ratio were calculated.

Results: Age distribution of patients was calculated which revealed most patients i.e., 43.3 % (n = 65) in age group 41 to 60 years with mean and standard deviation to be 13.22. Statistical analysis for diagnostic accuracy revealed 72.5 % (n = 108) true positive, 9.3 % (n=14) as false positive, 13.3% (n=20) as true negative and 5.3 % (n=8) as false negative. Calculations showed positive predictive value of 96.4 %, negative predictive value of 71.42%, sensitivity of 93.1%, specificity of 83.3%, diagnostic accuracy of 85.3% and a diagnostic odds ratio of 19%.

Conclusion: Results showed a high positive predictive value of HRCT in PCR negative patients with high clinical suspicion of COVID-19 by taking their antibody titre as gold standard.

Key Words: Positive predictive value, HRCT, COVID-19, PCR,

COVID-19 caused by Severe Acute Respiratory Syndrome Corona Virus 2 is a deadly disease which started in December 2019 in the city of Wuhan, China. Corona virus is a member of enveloped single stranded RNA viruses.[1,2] SARS-COV is one of the deadly strains of human corona viruses with a mortality rate of 3.4%.[3,4] The mode of transmission is via respiratory droplets with an incubation period of four days. It presents as fever, cough, and body myalgias clinically which is represented as ground glass haze with interlobular septal thickening and crazy paving pattern on HRCT (High Resolution Computed Tomography) leading to respiratory failure and mortality. The work is still in progress to find a cure for COVID-19 which further highlights early detection and quarantine of COVID-19 patients.

Reverse Transcriptase polymerase chain reaction (RT-PCR) is considered as the diagnostic test for COVID-19. It is performed on nasopharyngeal or

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oropharyngeal swabs, sputum, blood samples, body fluids, stool samples and bronchoalveolar lavage fluids. PCR has low sensitivity and relatively high number of false negative results leading to wrong labelling of the patient as being healthy and non-infectious. This can lead to further spread of infection in terms of negligence on behalf of the patient. According to a study conducted in the center for Academic primary care, Boston, UK, high pretest probability of 90% in terms of clinical symptoms has a 74% chance of patient suffering from COVID-19. Even with two negative tests with high pre-test probability, this risk is still 74%.[5]

HRCT has become the diagnostic modality for the management and assessment of respiratory conditions and especially for COVID-19. It also helps in the management of the patient.[6,7] Due to excessive load and variability in testing methodology for RT-PCR, negative test result is also common. In these cases, HRCT can help in the early detection and management of the patient. According to a study conducted by Buyun Xu, HRCT has a sensitivity of 92% and specificity of 25%(8). The objective of our study was to find the positive predictive value of HRCT in patients who have negative PCR results but their pretest probability to have COVID-19 is very high in terms of clinical signs and symptoms. It can help in proper management and early isolation of the patient which can improve the prognosis of the patient and help in controlling the spread of the disease.

METHODOLOGY

We did a retrospective study with a sample size of 150 patients at the Department of Diagnostic Radiology, Jinnah Hospital Lahore, Pakistan. The study was done in a period of six months i.e., from September 2020 to February 2021 when COVID-19 was at its peak in Pakistan. The study included patients aged 18-80 years. They had all the clinical symptoms and were highly suspected of having COVID-19 but their lab specimens showed either single or double PCR negative results. Pregnant patients and PCR positive patients were excluded from the study. Their HRCT were retrieved from the system done on Philiphs. Their HRCT were examined and reported by two senior radiologists having vast experience in reporting CT chest. Positive findings included peripheral and basilar ground glass haze with interlobular septal thickening. Severity was categorized as CO-RADS, a CT scoring system proposed by Dutch association of radiology. Their antibody titre was traced and was used as gold standard for the study. Statistical analysis was done by SPSS windows package version 20. Quantitative variables like age were presented in the form of mean +/- standard deviation (SD).

RESULTS

150 patients with negative PCR results were included in the study to find out the positive predictive value of HRCT in establishing the diagnosis. Antibody titre of these patients was evaluated post treatment for confirming the findings.

Age distribution of these patients was calculated. It showed majority of patients i.e., 43.3 % (n = 65) in between 41 to 60 years. 30.0% (n=45) were in age group 61 to 80 years and 27 % (n=40) patients were in age group 18 to 40.

Calculating the diagnostic accuracy of HRCT in predicting COVID-19 with negative PCR results showed 72.5 % (n=108) true positive, 9.3% (n=14) as false positive, 13.3% (n=20) as true negative and 5.3% (n=8) as false negative. Results showed a positive predictive value of 96.4%, negative predictive value of 71.4%, sensitivity of 93.1%, specificity of 83.3%, diagnostic accuracy of 85.3% and a diagnostic odds ratio of 19%.

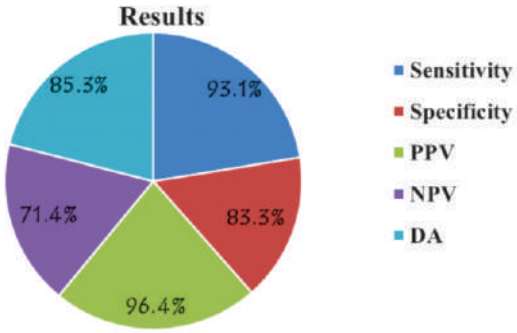
Table 1: *Age Distribution of Patients*

Age in Years 18 to 80	Number of Patients	Percentage
18 to 40	40	27
41 to 60	65	43.3
61 to 80	45	30
Total	**150**	**100**
Mean and SD	**50 ± 13.2**	

Table 2: *Diagnostic Accuracy of Hrct in Pcr Negative Patients With High Clinical Suspicion of Covid-19 Using Antibody Titre as Gold Standard*

HRCT	Positive		Negative		Total	
Positive	**(a) True Positive**	**Percentage**	**(b) False Positive**	**Percentage**	**a + b**	**Percentage**
	108	72.5	14	9.3	122	81.3
Negative	**(c) False Negative**	**Percentage**	**(d) True Negative**	**Percentage**	**c + d**	**Percentage**
	8	5.3	20	13.3	28	18.7
Total	**a + c**	**Percentage**	**b + d**	**Percentage**	**a + b + c +d**	**Percentage**
	116	**77.3**	**34**	**22.6**	**150**	**100**

Sensitivity = a/ (a+c) x 100 = 93.1 %; Specificity = d/ (b+d) x 100 = 83.3 %
Positive Predictive value (PPV) = a /(a+b) x 100 = 96.4 %
Negative Predictive value (NPV) = d / (c+d) x 100 = 71.4%
Diagnostic Accuracy (DA) = a +d / a+b+c+d = 85.3 %
Diagnostic odds ratio (DOR) = (a/c)/(b/d) = 19 %.



Pie Chart *Depicting the Positive Sensitivity, Specificity, PPV, NPV and DA*

DISCUSSION

Since the beginning of COVID-19 epidemic, the number of people suffering from this disease has risen to more than 95 million worldwide with over 2.02 million deaths to date. RT-PCR is considered as the diagnostic tool for COVID. However, according to a study conducted by Maulin et al. (2020) at Temple university hospital, Philadelphia, 20% of admissions in the hospital with suspicion of COVID-19 had negative PCR test results but had positive findings of COVID-19 on HRCT. Further, these patients showed clinical signs and other laboratory values as antibody titre and D-Dimers which also pointed towards the diagnosis.[9] Oropharyngeal and nasopharyngeal swabs are currently the method of performing RT-PCR with a sensitivity of 60%.[10] Although RT-PCR serves as the diagnostic modality, its false negative results are not rare. Similarly, during the second peak vast need for PCR laboratory kits and variability in laboratory techniques on account of technicians requires help from HRCT in supporting the diagnosis. Also, in some patients time variability in acquiring the specimen also results in negative results. All these scenarios have increased the importance of HRCT in establishing the diagnosis of COVID-19.

HRCT plays a key role in the diagnosis of COVID-19. In a study conducted by Wu et al. (2020) sensitivity of HRCT was found to be about 69% although in that study severity of symptoms was just 3.8% in PCR positive patients.[11] Common CT findings included bilateral ground glass opacification, consolidation, and interlobular septal thickening. In our study we divided the patients according to their ages with maximum number of patients n=65 in between 41 to 60 years with severity of CORAD 4. Old age group n=45 showed severity of CORAD 4-5. Since PCR test was negative in all these patients, their HRCT was examined and reported by senior radiologists. Bai et al. 2020) investigated the role of the radiologist in reporting HRCT images of COVID-19 which found out that radiological experience at reporting greatly affects the diagnostic accuracy of HRCT.[12] Our results concluded a sensitivity of 93.1% and a specificity of 83.3% for HRCT in predicting COVID-19. The study by Buyun Xu(8) (2020) reported a sensitivity of 92% and specificity of 25%. The decrease in specificity is due to overlap of findings with other respiratory conditions. Also, in some other cases as in our study, some patients never give positive PCR results. It might be due to inappropriate time of acquisition of the sample or due to inadequate sample. There are some individual factors as variability in age of patients and severity of

symptoms. In these cases, HRCT serves as the diagnostic modality. Our study showed a PPV of 96.4% and a diagnostic accuracy of 85.3%. However, in this time of epidemic, sensitivity and PPV are much more important as it results in early detection and isolation of patients. British Society of Thoracic Imaging also suggests the importance of the role of the radiological assessment especially in cases of diagnostic uncertainty.[13]

In addition to the diagnostic role of HRCT, it also plays a role in the management of the patient. Early detection helps in the start of proper treatment and quick recovery. Follow up of the patients can also be done by CT. Pan et al. (2020) categorized the patients in four categories according to severity on HRCT i.e., early, progressive, peak and absorption.[14] Hence HRCT has got a very important role in the diagnosis and management of patients with high sensitivity and positive predictive values.

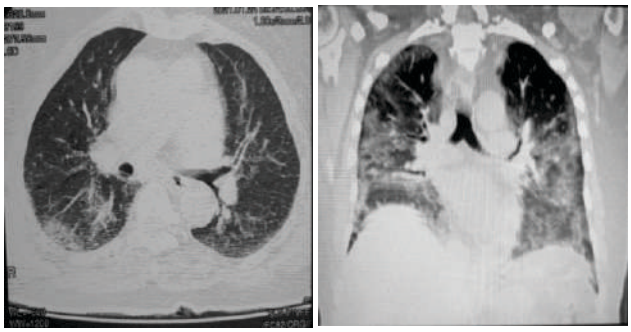


Figure 1(a&b): *Axial and Coronal Sections of HRCT-Chest showing Ground Glass Haze with Interlobular Septal Thickening of CORAD-3 Severity in Figure a and CORAD-4 in Figure b.*

CONCLUSION

Results showed a high predictive value of HRCT in PCR negative patients with high clinical suspicion of COVID-19 by taking their antibody titre as gold standard.

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COMPARISON OF THE EFFICACY OF PREGABALIN AND GABAPENTIN IN RELIEF OF UREMIC PRURITIS

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Abstract

Objective: To compare the efficacy of pregabalin and gabapentin in terms of relief of uremic pruritis.

Methodology: Patients fulfilling the selection criteria were enrolled in the study. Informed written consent was taken. Demographic details (age, name, gender & address) were recorded. Patients were randomly divided into two groups by using computer generated random number table. Patients in group A were given pregabalin (Cap. Zeegap 25mg/day) and patients in the group B were given gabapentin (Cap. Neogab 100mg/day) for one month. Findings were recorded on a performa.

Results: 220 patients meeting the inclusion criteria were included in the study. The minimum age was 12 years and maximum was 80 years (Mean 46.76 ± 16.137 years). Mean duration of disease was 3.4 ± 2.310 years. In group A the itch score on visual analogue scale at baseline was 6.28 ± 1.402 and after four weeks of treatment it was 4.52 ± 1.728 (p=0.0001). In group B the itch score at baseline was 6.45 ± 1.372 and after four weeks it was 4.30 ± 1.518 (p=0.0001). In group A 51.8% patients were below 50 years while in group B 54.5% patients were below 50 years. 49.1% of the study population was male and 50.9% was female. 70% patients in group A had disease duration of less than 5 years while 82.7% patients in group B had disease duration of less than 5 years. In group A pregabalin was effective in 69.1% patients and in group B gabapentin was effective in 80.9% patients (p= 0.043). In age less than 50 years pregabalin was effective in 78.9% patients and gabapentin was effective in 80% patients (p=0.888). In age more than 50 years pregabalin was effective in 58.5% patients and gabapentin was effective in 70.7% patients (p=0.0009). In the male population pregabalin was effective in 70.7% patients while gabapentin was effective in 84% patients (p=0.102). In the female patients pregabalin was effective in 67.3% patients and gabapentin was effective in 78.3% patients (p=0.189). In patients with disease duration less than 5 years pregabalin was effective in 68.8% patients and gabapentin was effective in 80.2% patients (p=0.244).

Conclusion: Gabapentin 100 mg per day was equally effective as pregabalin 25 mg per day in relieving the itching in ESRD patients receiving hemodialysis. However gabapentin was more effective in patients above 50 years of age.

Key Words: Haemodialysis, Chronic kidney disease, End-stage renal disease, Uremic pruritis, Visual analogue scale.

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Chronic kidney disease (CKD) is increasingly recognized as a global health problem. Newer and effective strategies are needed for the management of this condition.[1]

Of all systemic disorders, uremia is the most important cause of pruritus. Pruritus affects up to 90% of patients undergoing haemodialysis and the symptoms range from localized and mild to generalized and severe. Among the dermatological abnormalities

associated with end-stage renal disease, pruritus is the most prevalent.[2] The unremitting symptoms stop the patient from sleeping or relaxing. Haemodialysis patients with moderate or severe pruritus are more likely to feel drained or depressed and have a 17% higher mortality risk.[3]

Uremic pruritus (UP) can present somewhat variably, although it tends to affect large, discontinuous but symmetric areas of skin and to be most symptomatic at night. A variety of alternative systemic or dermatologic conditions should be considered, especially in patients with asymmetric pruritus or other atypical features.[4] Most frequently involved body surface areas include back, limbs, chest and face however can be generalized also.[5]

The mechanism underlying pruritus is poorly understood. Current theories include secondary hyperparathyroidism, divalent ion abnormalities, histamine allergic sensitization, proliferation of skin mast cells, iron deficiency, xerosis, neuropathy, cytokines, nitric oxide and opioid system involvement or some combination of these.[6]

It has become increasingly evident that central transmission and sensitization processes similar to those observed in chronic pain are important mechanisms of pruritus. Uremic Pruritus is a sort of neuropathic itch.[7]

There are different treatment options available for the management of uremic pruritus in the form of antihistamines, local emollients, charcoal, phosphate binders etc. Improved dialysis efficacy and use of biocompatible membranes has lead to improvement in symptoms in dialysis patients. Recent literature shows the use of gabapentin and pregabalin in the treatment of uremic pruritus.[8] In one study gabapentin relieved itching in 66% of the patients at a dose of 100mg/day and pregabalin relieved itching in 81% of the patients at a dose of 25mg/day. Gabapentin and pregabalin are used in treatment of different types of neuropathic pains like peripheral diabetic neuropathy, post-herpetic neuralgia and trigeminal neuralgia.[9]

At present no effective treatment is available for relief of uremic pruritus and local data on this subject is limited. The rationale of this study is to find a better drug for relief of UP which is a very disabling problem for patients on hemodialysis.

METHODOLOGY

Patients fulfilling the selection criteria were enrolled in the study from Nephrology Department of Allied Hospital Faisalabad. Informed consent was taken. Demographic information (age, name, gender & address) recorded. Patients were randomly divided into two groups by using computer generated random number table, patients in group A were given pregabalin (capsule zeegap25mg/day) and patients in the group B were given gabapentin (capsule neogab 100 mg/day). Both the drugs were given for one month and symptoms were recorded on visual analogue scale. Findings were recorded on a performa.

Collected data was entered and analyzed in the SPSS version 17. Mean with standard deviation were calculated for quantitative variables like age, VAS score at baseline and 4 weeks. Frequency and percentage were calculated for categorical variables like gender and relief of itching. Chi-squire test was used to compare relief of itching between two groups. Effect modifiers like age, gender and duration were controlled by stratification. Post stratification chi-square test was applied. P value ≤ 0.05 is significant.

RESULTS

Two hundred and twenty patients meeting the inclusion criteria were included in the study. The minimum age was 12 years and maximum was 80 years with a mean age of 46.76 ±16.137 years (Table 1). The mean duration of disease was 3.4 ± 2.310 years (Table 2).

The study population was divided into two groups. Each group contained 110 patients. Patients in group A were given pregabalin 25 mg per day and those in group B were given gabapentin 100mg per day (Table 2).

In group A the itch score on visual analogue scale at baseline was 6.28 ± 1.402 and after four weeks of

treatment it was 4.52 ± 1.728 with a p-value of 0.0001. In group B the itch score at baseline was 6.45 ± 1.372 and after four weeks it was 4.30 ± 1.518 with a p-value of 0.0001 (Table 3).

In group A 51.8% of population was below 50 years while in group B 54.5% of population was below 50 years (Table 4). Out of total patients 49.1% were male and 50.9% ware female (Table 5). Disease duration of less than 5 years was 70.0% in group A and 82.7% in group B (Table 6).

In group A pregabalin was effective in 69.1% of the population and in group B gabapentin was effective in 80.9% of the population. The chi-square and p-values were 4.097 and 0.043 respectively (Table 7).

In age less than 50 years pregabalin was effective in 78.9% of the population and gabapentin was effective in 80% of the population with a p-value of 0.888. In age more than 50 years pregabalin was effective in 58.5% of population and gabapentin was effective in 70.7% of population with a p-value of 0.0009 (Table 8).

In the male population pregabalin was effective in 70.7% of population while gabapentin was effective in 84% of population with a p-value of 0.102. In the female population pregabalin was effective in 67.3% of population and gabapentin was effective in 78.3% of population with a p-value of 0.189 (Table 9).

In patients with disease duration of less than 5 years pregabalin was effective in 68.8% of population and gabapentin was effective in 80.2% of population with a p-value of 0.244 (Table 10).

Table 1: *Distribution of Age and Disease Duration*

Variables	N	Min.	Max.	Mean	Std. Deviation
Age	220	12	80	46.76	16.137
Disease duration	220	1	9	3.46	2.310

Table 2: *Age and Duration of Disease Distribution According to Drugs*

Group	Variables	N	Min	Max	Mean	Std. Deviation
Group A	Age	110	12	80	46.08	16.052
	Duration of disease	110	1	9	3.75	2.520
Group B	Age	110	17	80	47.44	16.267
	Duration of disease	110	1	8	3.17	2.049

Table 3: *Itch Score in both Groups*

Group	Variables	N	Mean	Std. Deviation	p-value
Group A	VAS at baseline	110	6.28	1.402	0.0001
	VAS after 4 weeks	110	4.52	1.728	
Group B	VAS at baseline	110	6.45	1.372	0.0001
	VAS after 4 weeks	110	4.30	1.518	

Table 4: *Age Distribution*

Age	Group A	Group B	Total
< 50 years	57 (51.8%)	60 (54.5%)	117 (53.2%)
⩾ 50 years	53 (48.2%)	50 (45.5%)	103 (46.8%)
Chi-square value = 0.164		p-value = 0.685	

Table 5: *Gender Distribution*

Gender	group A	group B	Total
Male	58 (52.7%)	50 (45.5%)	108 (49.1%)
Female	52 (47.3%)	60 (54.5%)	112 (50.9%)
Chi-square value = 1.164		p-value = 0.281	

Table 6: *Duration of Disease in both Groups*

Disease duration	Group A	Group B	Total
< 5 years	77 (70%)	91 (82.7%)	168(76.4%)
⩾ 5 years	33 (30%)	19 (17.3%)	52 (23.6%)
Chi-square value = 4.936		p-value = 0.026	

Table 7: *Efficacy of Drug*

Efficacy	Group A	Group B	Total
Yes	76 (69.1%)	89 (80.9%)	165 (75%)
No	34 (30.9%)	21 (19.1%)	55 (25%)
Chi-square value = 4.097		p-value = 0.043	

Table 8: *Efficacy According to Age*

Age	Efficacy	Group		Total	p-value
		Group A	Group B		
< 50 years	Yes	45 (78.9%)	48 (80%)	93	0.888
	No	12 (21.1%)	12 (20%)	24	
	Total	**57**	**60**	**117**	
⩾ 50 years	Yes	31 (58.5%)	41 (82%)	72	0.009
	No	22 (41.5%)	9 (18%)	31	
	Total	**53**	**50**	**103**	

DISCUSSION

Pruritus is a common symptom in patients with end-stage renal disease (ESRD). In older series, up to 90% of patients were affected with pruritus, but now 20% to 50% are affected.[1-3] Pruritus occurs independent of the cause of the ESRD, and patients on both peritoneal and hemodialysis experience pruritus at similar rates. All races, both genders and all ages can develop ESRD pruritus.[4] Nephrologists have recognized and documented significant impact of itch on ESRD patients' quality of life. In addition, pruritus is an independent predictor of increased mortality, probably because of effect on a patient's quality of sleep.

Table 9: Efficacy According to Gender

Gender	Efficacy	Group		Total	p-value
		group A	group B		
Male	Yes	41(70.7%)	42(84%)	83	0.102
	No	17(29.3%)	8 (16%)	25	
	Total	**58**	**50**	**108**	
Female	Yes	35(67.3%)	47(78.3%)	82	0.189
	No	17(32.7%)	13(21.7%)	30	
	Total	**52**	**60**	**112**	

Table 10: Efficacy According to Duration of Disease

Disease duration	Efficacy	Group		Total	p-value
		Group A	Group B		
< 5 year	Yes	53(68.8%)	73(80.2%)	126(75%)	0.089
	No	24(31.2%)	18(19.8%)	42(25.0%)	
	Total	**77**	**91**	**168**	
⩾ 5 year	Yes	23(69.7%)	16(84.2%)	39(75%)	0.244
	No	10(30.3%)	3(15.8%)	13(25%)	
	Total	**33**	**19**	**52**	

The pathogenic basis of pruritus in renal failure is unknown. The renal failure must be severe to be associated with pruritus. The resolution of itch, albeit slowly in some cases, after renal transplantation suggests that a factor normally removed by the kidney but not effectively removed during dialysis is playing a role. Xerosis is common in patients with ESRD and may contribute to pruritus. ESRD pruritus is associated with elevated C-reactive protein and other inflammatory cytokines, suggesting there is an inflammatory component in this form of pruritus. The abnormalities of calcium metabolism that occur in the setting of ESRD may lead to formation of calcium phosphate crystals in the skin. These crystals may stimulate itch receptors. As in hepatic pruritus, endogenous opioids may be important in mediating the itch associated with ESRD. Once chronic pruritus has occurred, there may be secondary changes in nerves in the skin and perhaps the central nervous system which enhance the perception/sensation of itch (central sensitization).

The clinical characteristics of ESRD pruritus are variable.[1] The pruritus may be constant or intermittent. The back is the most commonly affected area, but arms, head, and abdomen are also commonly affected. Excoriations with no primary lesions and sparing of the butterfly area of the back are typical. Patients with ESRD, especially if attributable to diabetes mellitus, frequently develop keratotic nodules that on biopsy show a perforating disorder. These represent prurigo nodules and are a marker for severe and long-term pruritus.

The therapy for renal pruritus is often rewarding because the dermatologist has numerous options, some of which are usually effective. Treatment begins with topical agents. Treatment of xerosis with moisturization and gentle skin care can be quite beneficial.[5] The addition of soothing topical containing menthol or pramoxine can be tried.[6] Topical capsaicin can also be beneficial for patients with localized pruritus. Topical tacrolimus dramatically reduced pruritus by 80% in one study of patients with ESRD pruritus, but the vehicle gave a similar result.[7] For localized pruritus, this could be considered as an option, but for widespread itch, systemic absorption and cost are limitations.

Standard first and second generation antihistamines are usually of limited value. However, doxepin 10 mg once or twice daily has been shown effective.[8] Blood levels can be monitored enhancing safety. Mirtazapine 15-30 mg/d is another option. Both montelukast and cromolyn sodium, agents used in allergic disorders, have shown efficacy in ESRD pruritus.[9,10]

Adequate and effective dialysis is critical in alleviating pruritus in ESRD.10 Controlling calcium and phosphorus seem to be particularly important.[11]

In addition, treating the underlying iron deficiency may alleviate itch.[12]

The administration of 300 mg of gabapentin after each dialysis has been shown in multiple studies to improve ESRD pruritus.[13] The response to treatment, although not universal, is usually durable, and when effective is a very safe new addition for the treatment of ESRD pruritus. Pregabalin can be similarly effective. Recently, the use of neuroleptic agents, such as gabapentin and pregabalin (PG), has massively increased for the management of treatment-resistant UP. Neuroleptic agents such as gabapentin have good effectiveness for the treatment of pruritus that is resistant or non-responsive to topical and other systemic treatment options.[12] However, pregabalin (PG) has been found to be effective in providing relief for the patient's condition in some situations where patients are unable to tolerate gabapentin.[13,14] Gabapentin and PG have drastic differences in their pharmacokinetics and pharmacodynamics. The oral absorption of gabapentin is slower than PG, which attains its plasma peak concentration within 1 hour .[15] Furthermore, the dose-dependent concentration increase is not a characteristic of gabapentin. However, the bioavailability of gabapentin reduces from sixty to 33.0% when the dose increases from 900 mg/day to 3600 mg/day.[16] For PG, the bioavailability remains more that 90% regardless of the dose increase. These pharmacokinetic benefits provide a pharmacodynamics edge to PG over gabapentin. However, gabapentin is often not tolerated by ESRD patients due to their compromised renal functions, poor oral absorption and the low bioavailability of gabapentin, which is another challenge. Therefore, the use of higher gabapentin doses for ESRD patients has led to an increased risk of adverse events associated with its use.[14] PG is superior to gabapentin in this regard. A recent longitudinal study conducted by Shavit et al. (2013) reported the therapeutic effectiveness of PG at a dose of 25–50 mg/day among uremic patients with treatment-resistant pruritus who had shown resistance to antihistamines and emollients.[17] Additionally, Aperis et al. (2010) and Rayner et al. (2013) reported the effectiveness of PG at a dose of 25 mg/day among ESRD patients with treatment-resistance pruritus,[13,18] with the severity of the pruritus markedly reduced among the patients treated with PG.

Ultraviolet B (UVB) phototherapy, especially broadband UVB, is frequently effective for ESRD pruritus.15NB-UVB and UVA alone do not appear as effective. Starting at three times per week and reducing to maintenance once or twice weekly can often control the pruritus.

The standard opiate antagonists naltrexone and butorphanol can be tried but have not been universally beneficial. Nalfurafine, a kappa agonist, demonstrated modest improvement and is a potential new option for treatment of ESRD pruritus.[16]

In refractory patients, novel approaches may be useful. The administration of 1 mg of ganisetron orally twice a day can be effective, but another serotonin type 3 receptor antagonist, ondansetron, is ineffective.[17] The administration of 600 mg of pentoxyfilline once after each dialysis, although poorly tolerated by some patients, was reasonably effective in a small series.[2] Thalidomide at a dose of 100 mg daily has reduced pruritus rapidly in one series and should be considered in refractory patients, especially those with prurigo nodules.[18] In the most severely affected patients, 5 mg of nicergoline intravenously during dialysis can be tried.[3] Acupuncture and other physical modalities may provide benefit.[1,19]

This study compared the use of gabapentin with pregabalin in ESRD patients for the relief of pruritis. In both study groups the itch score at baseline was comparable. After four weeks of treatment both the groups showed significant reduction in itch score from baseline. In the subgroup analysis population aged more than 50 years gabapentin was more effective in relieving the itch as compared to pregabalin (p-value 0.0009). In all other groups there was no significant variation in both the drugs in reducing the itch score.

A study of Rayner et al compared gabapentin with pregabalin. They also found both drugs to be

equally effective in terms of relief of itching. However they didn't randomized the use of drugs into two groups, rather switched the patients from gabapentin to pregabalin if they experienced intolerable side effects with gabapentin. Also all the study population was not on dialysis as compared to our study.

A study by Solak et al also yielded similar results. They conducted a 14 week randomized crossover trial in hemodialysis patients comparing gabapentin and pregabalin. They found both the drugs equally effective in relieving itch. However they used a higher dose of pregabalin as compared to our study. Also they used gabapentin in a higher dose but after every dialysis. However they had a smaller sample size.

A study by Gunal et al also evaluated the role of gabapentin in relief of itching in hemodialysis patients. They also found significant reduction in itching with use of gabapentin after every dialysis. However it was a placebo controlled trial and didn't compare gabapentin with pregabalin. Also the study population was very small.

Naini et al also found gabapentin to be effective in relief of itching in hemodialysis patients. However the sample size was small and it was also a placebo controlled trial.

A study by khan et al also showed significant improvement in itching with use of pregabalin. However they used higher dose of pregabalin (75 mg after every dialysis), and also it was not a controlled trial.

Our study had few limitations. One limitation in this study was that we assessed UP only at specific time points and not on a daily basis. Nevertheless, the patients were interviewed by the researcher upon receiving dialysis to assess the presence or absence of UP. Additionally, no plasma concentrations were examined to confirm the results.

CONCLUSION

Gabapentin 100 mg per day was equally effective as pregabalin 25 mg per day in relieving the itching in ESRD patients receiving hemodialysis. However gabapentin was more effective in patients above 50 years of age.

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MANAGEMENT OF ACUTE ANKLE SPRAIN WITH BELOW KNEE CAST AND TUBULAR COMPRESSION BANDAGE

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Abstract

Background: Ankle sprains are most common sports injuries with significant proportion of the patients having persistent symptoms for months and even for years. Untreated sprain can result in osteocondral damage to talus and arthritis of ankle joint.

Objectives: To determine the effectiveness of two different treatment modalities below knee cast and tubular compression bandage in acute ankle sprain.

Methodology: This study was conducted at Department of Orthopedic surgery Services Hospital Lahore from December 2017 to October 2018. A total number of 100 patients having ankle sprain (all grades) were divided into two equal groups A and B. Mechanism of injury was planter flexion and inversion of foot. All patients were having first episode of injury to the ankle. Patients having chronic injury, chronic instability of the ankle, second episode of injury and associated fractures of ankle joint were excluded from the study. Radiograph including AP, Lateral and ankle mortise view were done to rule out the associated fractures. In 50% of the patients we applied the below knee cast and in remaining 50% patients the tubular compression bandage was applied for a period of 3 weeks. After 3rd week below knee cast and brace were removed and muscle strengthening exercises were started under supervision of physiotherapist. Each patient was followed for a period of 6 wks and karlsson score was used to assess the outcome.

Results: In group A there were 30 females and 20 males, while there were 24 females and 26 males in group B. In group A Right ankle was involved in 40 patients and left ankle in 10 patients while in group B, 35 patients had right ankle and 15 patients had involvement of left ankle which was statistically insignificant i.e. p value of > 0.05. The pain relief in group A was better than B at 6 week followup and swelling at 6 weeks in group A was significantly decreased, measured with ANNOVA test (p value of 0.000) as compared to group B.The karlsson score mean for below knee cast group was 78.2±5.3 and for tubular compression bandage it was 71±10.2 showing that there is significant difference in Karlsson score between two groups.

Conclusion: Short term immobilization in below knee cast offered a faster recovery in terms of pain and swelling than if patients are given only tubular compression bandage. Below knee cast has shown to have wide range of benefits.

Keywords: Ankle sprain, lateral ankle instability, chronic ankle instability,

Ankle sprain is one the most common traumatic ankle injury. It accounts for 10-30% of sports injuries. Female athletes are the most common sufferer. Its incidence is 5-6 per 1000 persons.[14] It can result in significant rate of recurrence and long term after effects. Repetitive ankle sprain and chronic instability can result in osteochondral damage to talus, lateral impingement of ankle and peroneal tendon attrition. The risk factors for injury are age, female gender, previous ankle sprain, athlete height, BMI, postural stability and exposure to contact sports. Indoor sports carry the greater risk of ankle sprain like basketball players. Ankle functions as a complex joint with contribution

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of talo-crural, subtalar and inferior tibio fibular joint. Each of these joints must be counted in the biomechanics and pathological deterioration caused by ankle sprain which can result in chronic ankle instability.[15] If it is not treated adequately it can later on end up in functional instability such as insufficiency in proprioception and loss of neuromuscular control. Chronic ankle instability has been attributed by repetitive episodes of ankle instability resulting from numerous ankle sprains with poor mechanical outcome of and functional loss.[9]

Lateral ankle sprain accounts for 85% of all ankle sprains. Mechanism of injury is inversion when foot is in planter flexed position.[16] This happens as a result of shift of body center of rotation over the landing or weight bearing of foot. The most common ligament injured is anterior talo-fibular ligament as this is the weakest of lateral ligamentous complex. In 65% of the cases there is complete rupture of anterior talo fibular ligament. While in 20% of the cases this injury occurs in the combination with calcaneo-fibular ligament. Calcaneo-fibular ligament is not only part of lateral ankle ligament but it also is a stabilizer of Sub-talar joint. Injury to this ligament implies injury to the Sub-talar joint. While the posterior talo-fibular ligament are less likely to sustain the injury. On the medial side of ankle joint the deltoid ligament complex, tibio-calcaneal ligament, tibio-navicular ligament and anterior tibio-talar ligament are injured with pronation and rotational movements of hind foot.[7]

Stabilizing ligament of distal tibio-fibular syndesmosis are antero-inferior, postero-inferior, transverse tibio-fibular ligament and tibio-fibular interosseous membrane and ligament.[8] Syndesmotic sprain occur with combined rotation of leg with ankle dorsiflexion. A lot of classifications have been proposed for lateral ankle sprain.[2] These are

Grade1 – There is stretching of ligament without macroscopic tear. Only little swelling and tenderness over the involved structures with minimal or no functional loss.

Grade 2 – has partial macroscopic tears in the ligament with moderate swelling with pain and tenderness over the involved structure. Here there is mild to moderate instability

Grade 3 – Sprain causes complete ligamentous rupture, significant hemorrhage and tenderness. Joint is unstable with abnormal movements and functional loss

A lot of controversies exist over the treatment of acute ankle sprain. For best treatment, a precise assessment of the status of individual ligaments is mandatory. To assess the status of this pathological instability especially in case of calcaneo-fibular ligament, one must have the stress views of the ankle joint. However these radiographs do not classify the degree of individual ligamentous injury. Other techniques for assessments of ligamentous injury are dynamic ultrasound imaging with high resolution and MRI for analysis of lateral ankle sprain.[3]

In the study done by Yeung et al. the dominant leg is 2.4 times more vulnerable to ankle sprain.[1] A lot of treatment options are available to treat acute ankle sprain. These include the below knee cast, tubular compression bandage, air cast brace, bledsow boot, functional treatment and surgical repair of lateral ankle ligaments complex and surgical management of ankle sprain.[10,11,12]

The below knee cast and air cast brace applied for ten days after the injury allows the swelling to subside, offer the cost effective alternative to tubular compression bandage. Below knee cast having the advantage to speed up the overall recovery for the ankle sprain.[4,5]

Biological ligamentous healing can be divided into three stages.[6] First is the phase of inflammation which last up to ten days after trauma followed by second phase which is phase of proliferation which last for 4-8 weeks and last of all is maturation phase which last until one year after the trauma.[7]

However lot of studies suggests that many patients develop the chronic problem after the injury that is chronic pain, recurrent swelling and chronic ankle instability. The high rate of failure of ankle sprain treatment might be explained by overlooked syndesmotic

or cartilaginous injury and the 2nd problem is inappropriate treatment of different ankle sprain grades during healing phase.[17]

Prolonged chronic instability of ankle joint can result osteoarthritis of the ankle joint,[13] however the number of patients suffering of osteoarthritis of ankle joint are small as compared to the knee joint osteoarthritis when compared with large group of patients.[10]

METHODOLOGY

This comparative study was conducted in the emergency Department of Orthopedic surgery at Services Hospital Lahore. The duration of the study was 11 months, from December 2017 to October, 2018. We included 100 patients in our study who were having ankle sprain (Grade 1,2,3). Patients having age of 16-60 years with no previous history of ankle fracture were divided into two equal groups A and B each group having 50 patients randomly. All these patients had history of trauma to the ankle. Mechanism of injury was planter flexion and inversion. All patients were having first episode of injury to the ankle. Patients having chronic injury and chronic instability of the ankle were excluded from the study. Similarly patients having second episode of injury and associated fracture of ankle were also excluded from the study. All patients underwent thorough history and clinical examination to determine the extent of ankle sprain. Radiograph including AP, Lateral and ankle mortise view were done to rule out the associated fractures. After the clinical examination and x-rays, each patient was given analgesia. In group A we applied the below knee cast and in Group B patients the tubular compression bandage was applied for a period of 3 weeks. After 3rd week below knee cast and tubular compression bandage was removed in OPD. Muscle strengthening exercises were started under supervision of physiotherapist. Patients were followed for next 3 weeks in OPD on weekly basis, and were assessed with Karlsson score which include pain, swelling, instability, stiffness, stairs climbing, running, work activities and use of support. Higher the score was better were the results. Data was assessed and analyzed by using SPSS version 20 and was expressed as mean±SD while the categorical data was expressed in terms of frequency. The visual analog score and swelling assessed by ANNOVA test and Karlsson score were revealed by using Student t-test. A p value of less than 0.05 was considered as significant for these statistical tests.

The Karlsson and Peterson Scoring System for Ankle Function

	Degree	Score
Pain	None	20
	During exercise	15
	Walking on uneven surface	10
	Walking on even surface	5
	Constant	0
Swelling	None	10
	After exercise	5
	Constant	0
Instability	None	25
	1-2 / year (during exercise)	20
	1-2 / month (during exercise)	15
	Walking on uneven ground	10
	Walking on uneven ground	5
	Constant (severe) using ankle support	0
Stiffness	None	5
	Moderate (morning, after exercise)	2
	Marked (constant, severe)	0
Stair climbing	No problems	10
	Impaired (instability)	5
	Impossible	0
Running	No problems	10
	Impaired	5
	Impossible	0
Work activities	Same as pre-injury	15
	Same work, less sports, normal leisure activities	10
	Lighter work, no sports, normal leisure activities	5
	Severe impaired work capacity, decreased leisure activities	0
Support	None	5
	Ankle support during exercise	2
	Ankle support during daily activities	0

RESULTS

In group A there were 30 females and 20 males,

while there were 24 females and 26 males in group B. Mean age in Group A was 34 ± 4 yrs while in group was 35±4 yrs. Right ankle was involved in 40 patients in group A and left ankle in remaining ten patients. In group B 35 patients had involvement of right ankle and 15 patients had involvement of left ankle which was statistically insignificant i.e. p value of > 0.05. The pain relief in group A was better than B at 6 week follow-up after removal of cast and regular physiotherapy and it was statistically significant (p-value< 0.005). The swelling before application of below knee cast and tubular compression bandage was not statistically significant (p value of 0.172) while swelling at 6 weeks in group A was significantly decreased and measured with ANNOVA test (p value of 0.000) as compared to group B. The karlsson score mean for below knee cast group was 78.2±5.3 and for tubular compression bandage it was 71±10.2 showing that there is significant difference in Karlsson score between two groups.

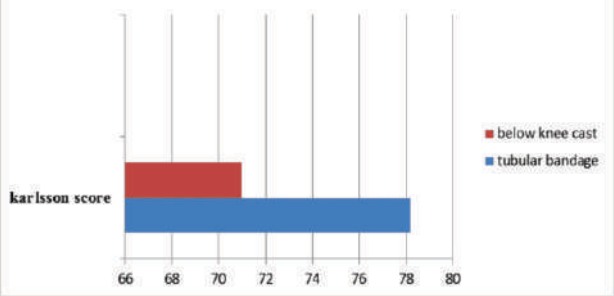
Demographic Data

	Group A	Group B
Age	34 ± 4	35±4
gender	Male 20 Female 30	Male 24 Female 26
Ankle involvement	Right 40 Left 10	Right 35 Left 15

Karlsson Score

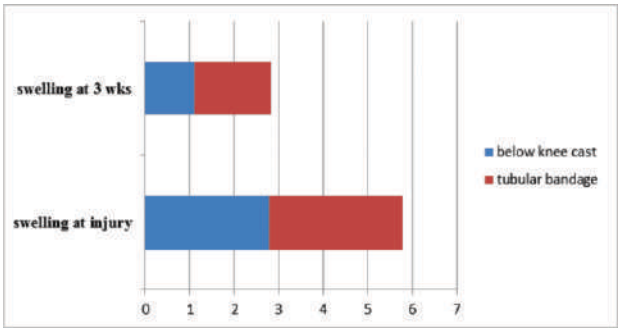
Type of treatment	Karlsson score at 6 weeks	p value
Below knee cast	78.2 ± 5.3	0.002
Tubular compression bandage	71.0 ± 10.2	

The karlssons score was 78.2 ± 5.3 for below knee cast and for tubular compression bandage was 71.0 ± 10.2 so there was significant difference in two groups.



Results of Swelling

Time of treatment	Below knee cast	Tubular compression bandage	ANNOVA test
At injury	**2.79** ± 0.6	**3.01** ± 0.065	**0.182**
At 6th week	**1.1** ± 0.49	**1.72** ± 0.50	**0.000**



DISCUSSION

Ankle sprain is one of the most common injuries presenting in emergency department. Still there is no gold standard for the treatment of this injury. Most of the orthopedic consultants rely on the clinical judgment and personal experience to treat these injuries.[17] In our study we evaluated the clinical effectiveness of below knee cast with tubular compression bandage for ankle sprain. Our study highlights the designs and methods of acute management of ankle sprain in the emergency department. 50% of our patients were managed with below knee cast and rests of 50% were managed by tubular compression bandage.[7] In the study conducted by Wolf Peterson et al. the majority of patens were with Grade 1, 2 and 3 ankle sprain and theses were treated without surgery. Indication for surgical repair should be based on individual basis. Therefore objective of our management was to determine the short term outcome of management of ankle sprain with goals of returning the patients to their pre injury status. Our study depicts that there was a significant difference in the Karlsson's score between the subjects who were treated with below knee cast (78.2±5.3) than those who were treated with tuular compression bandage (71.0±10.2).

In his study Lamb et.al deducted that the results of cast trial with short period of immobilization in a below knee cast has a faster recovery than if the patient is given only tubular compression bandage. Moreover

below knee cast was superior to other treatment modalities during the first 3 months, after that the functional treatment were equally effective after 9 months.[1]

In another study conducted by Dubin JC et.al showed that surgical treatment play a minor role in treatment of acute ankle sprain. Mostly these injuries can be treated with non-operative treatment. Cast immobilization speed up the healing and repair of soft tissue.[2]

In his study Craig C Young et.al.,[3] indicated that there are benefits to the use of below knee cast at least for 10 days. Below knee cast allows the swelling to subside (2-3 days) and offers a cost effective alternative to tubular bandage for acute severe ankle sprain. They advised that below knee cast has the advantages in terms of overall recovery at 3 months.

In another multicenter study conducted by Mustafa Uslu et.al.,[4] in J Am Podiatr Medical Assoc. 2015, july; came to the conclusion that short leg cast immobilization or splintage are effective in reducing the edema and increases the functional score of ankle.

The study conducted by Mathew W Cooke et.al.,[5] found that below knee cast and air cast brace offered cost effective alternative to tubular bandage for acute ankle sprains, the former having advantages of overall recovery at 3 months.

The study presented by Sara Lamb and colleagues in the randomized trial in which they evaluate the effects of four different types of immobilization devices i.e., tubi-grip compression bandage, Bledsoe boot, air cast brace and below knee cast in the treatment of ankle sprain. They concluded that below knee cast resulted in more rapid resolution of pain and have best recovery of ankle function in 3 months of follow up when compared with other treatment options.[5]

More recent evidences suggest that short period of immobilization for less than 10 days improve the overall function of ankle joint. It regresses the pain and edema induced by this injury.[6]

Ethical Approval by the hospital committee

This study was approved by institutional review board of Services Hospital Lahore

Limitation of Study

In our study the sample size was small and follow-up was also short. Another study should be done to include the large sample size and long follow-up.

Acknowledgement

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Conflict of Interest Author declared that there is no conflict of interest.

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COMPARISON OF COMPLETE BLOOD COUNT PARAMETERS BETWEEN TWO HAEMATOLOGY ANALYZERS: SYSMEX XP-100 AND SWELAB ALFA PLUS STANDARD

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Abstract

Background: This study was designed to compare the results of heamatological parameters between Sysmex XP-100 (B8958) and Swelab Alfa Plus Standard (114048) automated hematology analyzers.

Methodology: Hundred (100) blood samples were taken from Farooq Hospital westwood branch for the analysis of haematological parameters using the automated haematology analyzers. For analysis of results, we used passing bablok and bland altman deviation method.

Results: The two instruments showed good concordance in parameters of complete blood counts. Significant p-value was obtained <0.01 and r=0.98 which means correlation coefficient is good. A linear correlation was found in passing bablok regression analysis and bland altman deviation analysis exhibited that 95% results are within consistency limits.

Conclusion: In conclusion, the results of the two instruments are correlated and analyzers are reliable in performance. Both also provided flagging for abnormal platelet counts and it was further verified by manual slide method.

Key Word: Complete blood count, hematology analyzer

Performance of complete blood counts by modern automated hematology analyzers in present era has replaced the conventional manual method for different parameters and the microscopic differential count of leucocytes to detect haematological abnormalities.[1] Authentic automated blood cell quatification and identification is a big challenge at tertiary care hospital.[2] To meet this purpose, different haematology analyzers are available in market. We selected Sysmex Xp-100 and Swelab Alfa Plus Standard which are commonly used and their authorized distributors are available in market with proper backup services.

Sysmex XP-100 (B8958) is manufactured by sysmex corporation Japan. Impedence method is used for counting of white blood cells, red blood cells and platelets. For the hemoglobin content, non-cyanide haemoglobin method was used for detection.

Swelab Alfa Plus Standard (114048) is manufactured by Boule Diagnostics Sweden. Swelab alfa uses the impedance method to detect the number and volume distribution of white blood cells, red blood cells, and platelets and the hemoglobin concentration is measured by spectrophotometry.

Purpose of comparison of two instruments was to provide non stop facility of blood complete parameters. For assessment of difference and deviation in reporting, we use control materials and control materials were of same company.

METHODOLOGY

Therefore, in Aug 2020, Farooq Hospital West-

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wood Branch carried out the comparison of complete blood count of two instruments Swelab Alfa Plus Standard and Sysmex XP-100 and for backup purpose. The parameters analysed were Haemoglobin (HGB), Red blood cell count (RBC), Haematocrit (HCT), Mean cell volume (MCV), Mean corpuscular Haemoglobin (MCH), Mean corpuscular Haemoglobin concentration(MCHC), Platelets (PLT), White blood cell count (WBC), Polymorphs (POLY), Lymphocytes (LYM), and mixed cells (MXD).

Two instruments (sysmex and swelab) were operated for comparison of complete blood count parameters. Hundred samples were included in this study. Daily twenty samples were run on both instruments same time by same operator. Calibration of both analyzers was done by company engineer before running these samples. Normal and pathological controls (Sysmex lot# 03120821-03120822) (Swelab lot#22010-41,22010-42,22010-43) were run along with batch of samples and results were recorded and documented. The reagents, controls and calibrators used in the two instruments were original and operated according to the operating instructions provided by the instrument manufacturers.

Peripheral smear of samples having any abnormal value of platelet was seen by haematologist and any discrepancy was noted and highlighted. Flagging in any parameter on any instrument was rechecked and verified.

The results of the laboratory using Sysmex XP-100 and Swelab Alfa Plus Standard were selected. The two groups of test results that conformed to the normal distribution were tested by Bland Altman Deviation method. According to the different test items, the difference between the two instruments was compared. The difference was statistically significant at $P < 0.05$.

The test results of the two instruments were input into the MedCalc software for Bland-Altman analysis, and the deviation map was drawn. The Bland-Altman deviation map is a two-dimensional Cartesian coordinate, where the x-axis of the abscissa represents the average of the results of the two instruments, and the y-axis of the ordinate represents the percentage of the difference between the two instruments and the average value of the sample. The upper and lower horizontal lines in the figure represent the upper and lower limits of the 95% consistency limit, expressed by mean +1.96 SD and mean −1.96 SD, where mean is the average and SD is the standard deviation. If the scatter is evenly distributed on the lower side of the Y = 0 horizontal line, most of the scatter is within the consistency limit, and the consistency limit is narrower within the clinically recognized boundary value, indicating that the two instruments have higher consistency, and one can replace the other method. The difference was statistically significant at $P < 0.05$.

RESULTS

The results of the haematological parameters measured by Sysmex XP-100 and Swelab Alfa Plus standard were documented individually. The test items were Haemoglobin (HGB), Red blood cell count (RBC), Haematocrit (HCT), Mean Corpuscular Volume (MCV), Mean Haemoglobin Concentration (MCH), Mean Corpuscular Haemoglobin concentration (MCHC), Platelet count (PLT), white blood cell count (WBC), Polymorphs(POLY), Lymphocyte count (LYM) and Mixed Cells (MXD). According to the different test items, the test results of the two instruments were, respectively, tested by Altman method.

The measurement of HGB reported by both instruments were significantly correlated ®= 0.997, P-value < 0.001). Three values (3%) were found to be outlier according to Altman deviation analysis.

RBC count by both instruments were significantly correlated ®= 0.995, P-value < 0.001). Two values (2 %) were found to be outliers.

HCT reported by both instruments were significantly correlated ®= 0.993, P-value < 0.001). Two values (2 %) were found to be outliers.

MCV measurement by both instruments were significantly correlated ®= 0.986, P-value < 0.001).

MCH reported by both instruments were significantly correlated ®= 0.983, P-value < 0.001). Two

values (2 %) were found to be outliers.

MCHC measurement by both instruments were significantly correlated ®= 0.796, P-value < 0.001). One value (1 %) was found to be outlier.

Platelet count measured by both instruments were significantly correlated ®= 0.996, P-value < 0.001). One value (1 %) was found to be outlier.

WBC count reported by both instruments were significantly correlated ®= 0.993, P-value < 0.001). Two values (2 %) were found to be outliers.

Polymorph Neutrophil count reported by both instruments were significantly correlated ®= 0.978, P-value < 0.001). No value was found to be outlier.

Lymphocyte count by both instruments were significantly correlated ®= 0.993, P-value < 0.001). No value was found to be outlier.

Mixed cells reported by both instruments were significantly correlated ®= 0.368, P-value < 0.001). No value was found to be outlier.

Table 1: The Correlation Coefficient and P Value of each Parameter are Shown.

COMPARISON OF DATA

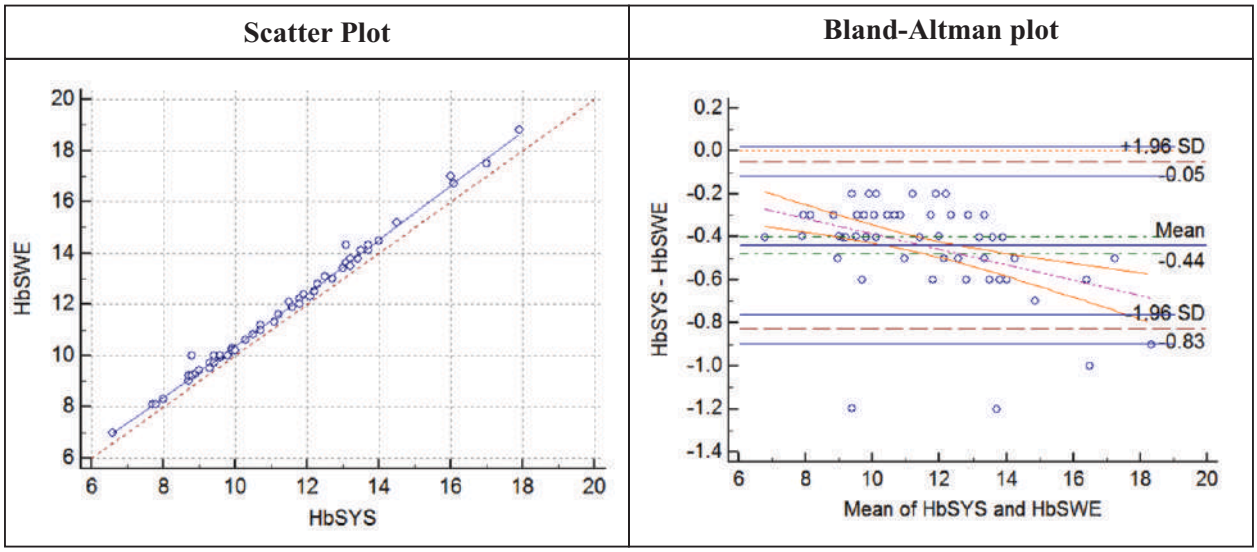
Variables	Correlation coefficient	P-value
Hb SYS Hb SWE	r= 0.997	<0.001
RBC SYS RBC SWE	r= 0.995	<0.001
HCT SYS HCT SWE	r= 0.993	<0.001
MCV SYS MCV SWE	r= 0.986	<0.001
MCH SYS MCH SWE	r= 0.983	<0.001
MCHC SYS MCHC SWE	r= 0.796	<0.001
PLT SYS PLT SWE	r= 0.996	<0.001
WBC SYS WBC SWE	r= 0.993	<0.001
POLY SYS POLY SWE	r= 0.978	<0.001
LYMPHO SYS LYMPHO SWE	r= 0.993	<0.001
MIX SYS MIXSWE	r= 0.368	<0.001

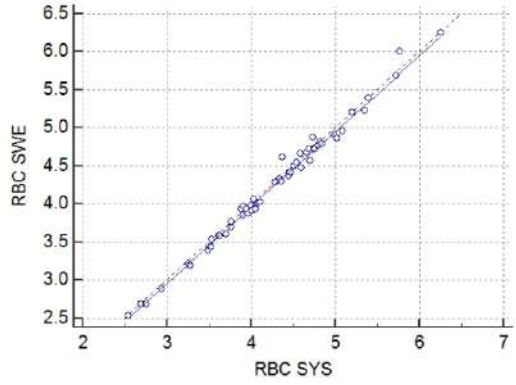
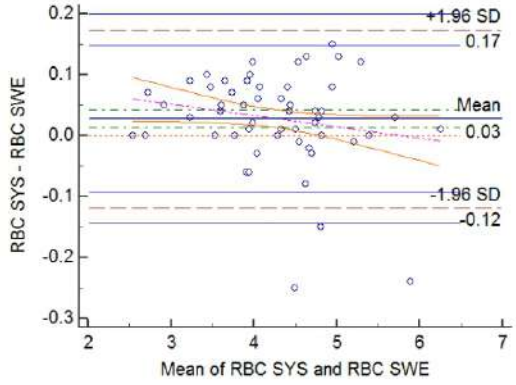
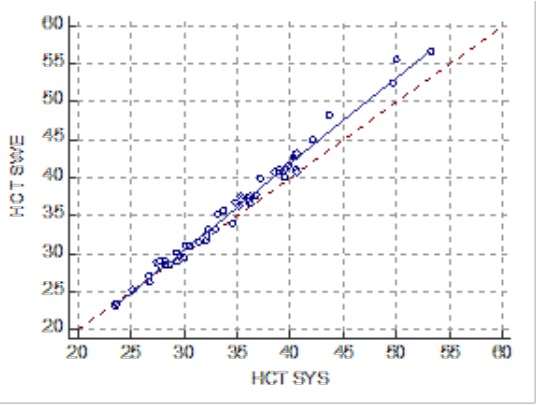
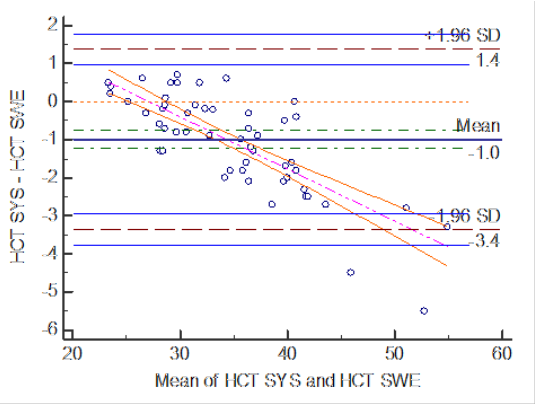
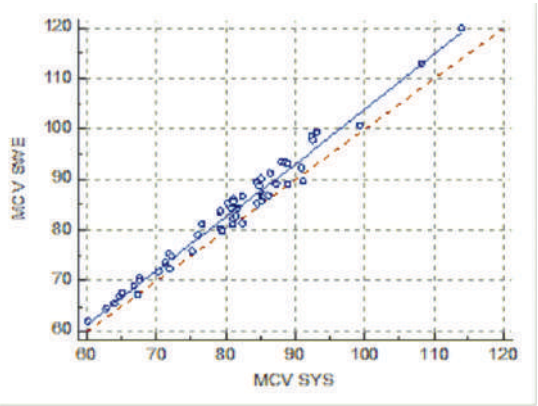
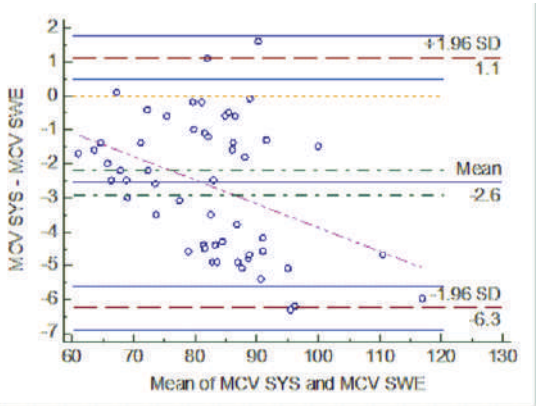
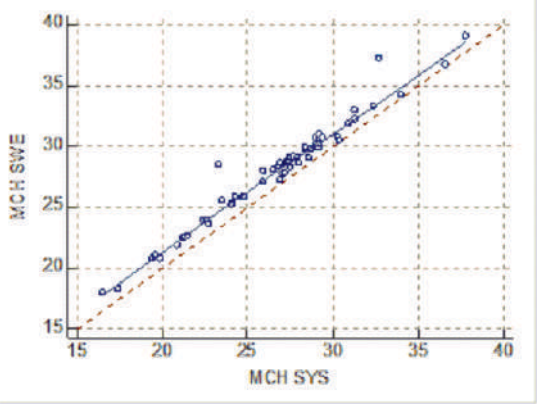
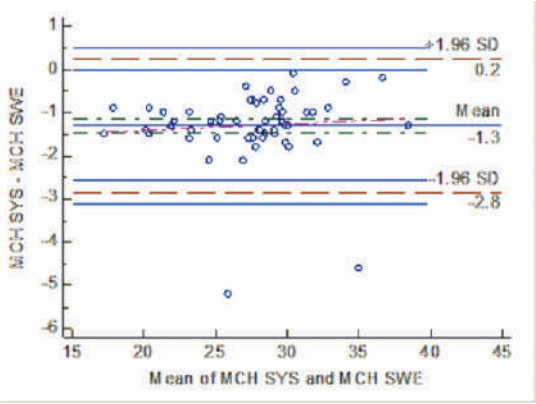
DISCUSSION

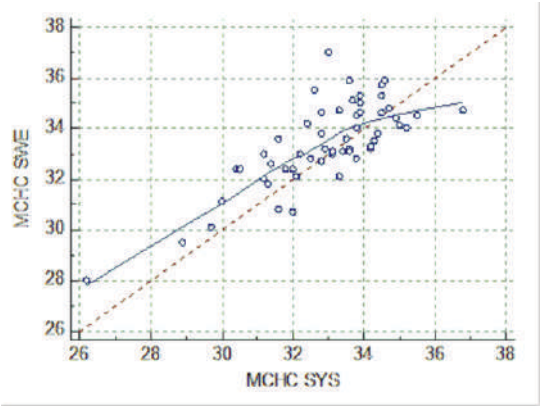
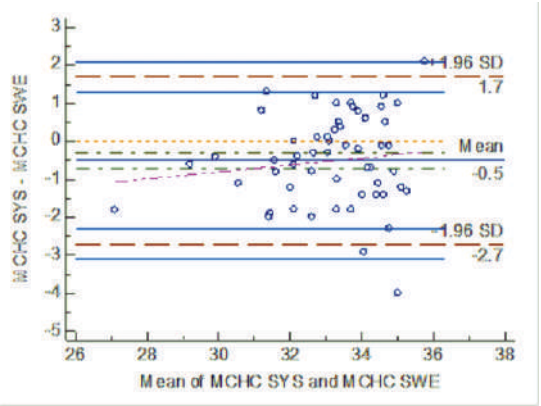
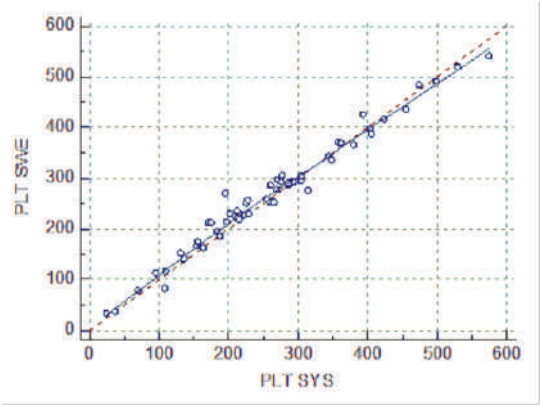
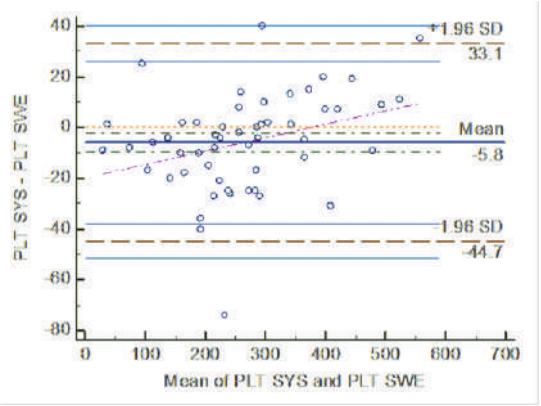
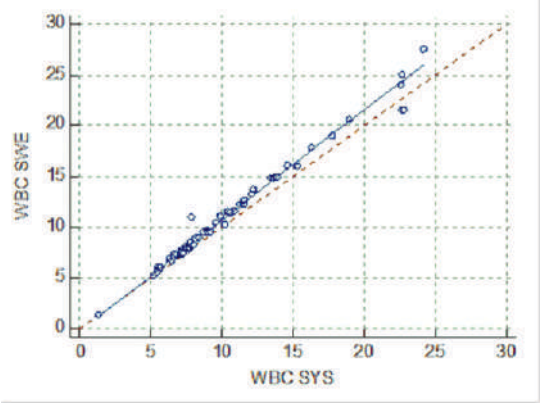
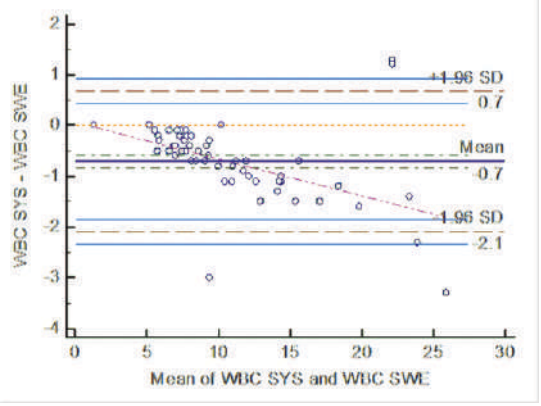
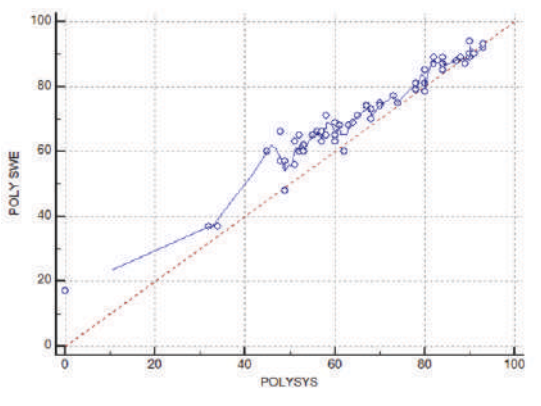
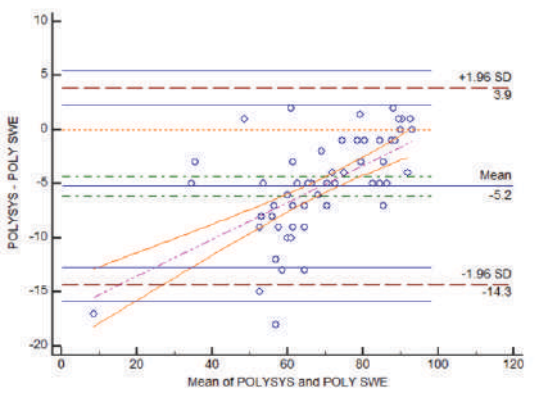
Different new techniques such as absorption spectrometry, impedance, and conductivity measurement, as well as sheath flow direct current detection are used in modern haematology analyzers. In addition, better analytical algorithms and recognition of pattern, automated cell differentiation is a cost-efficient and rapid method for complete blood cell count and leukocyte differential count.[3]

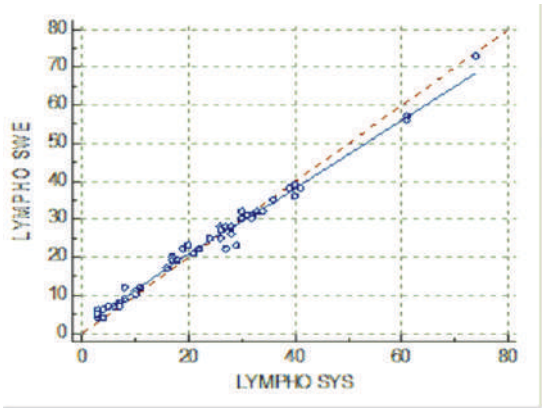
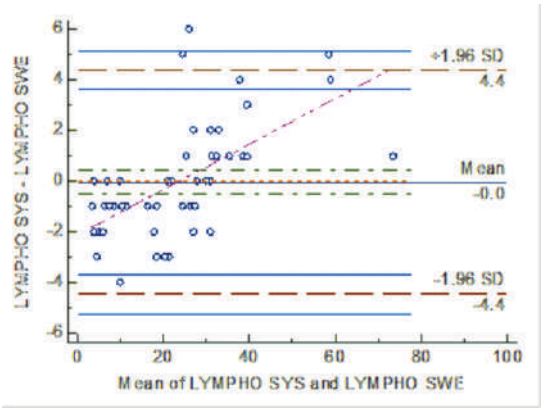
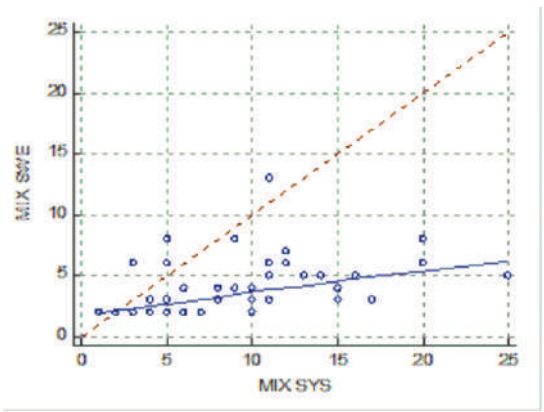
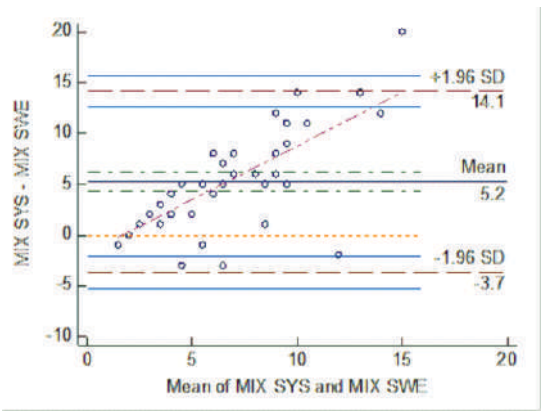
Advance technique for Automated morphology of different blood cells has developed to overcome interobserver variation and absence of uniform white

Figure: 1. *Scatter Plot and Bland-Altman Plot of Parameters*



Scatter Plot	Bland-Altman plot
	
	
	
	

Scatter Plot	Bland-Altman plot
	
	
	
	

Scatter Plot	Bland-Altman plot
	
	

cell distribution on peripheral blood slide and upgrade the efficiency and reliability of slide review.[4]

Based on well- established international standards of laboratory, comparison methods of measurements are generally applied to assess agreement or to evaluate bias by measuring the same quantity.[5] Cleophas TJ et al., proposed linear regression to authenticate quantitative tests of diagnosis. Two methods were used i.e Deming regression and Passing-Bablock regression. Passing bablock regression is non-parametric, vigorous, strong and more dependable because medians rather than means are used.[6,7] We applied this regression analysis to compare data obtained from these two analyzers and a linear correlation was observed. For the intercept of the regression equation, the 95% confidence interval showed that there is no systematic error and proportional difference between the two instruments. Correlation coefficient was found good.

Although to performe a statistical analysis with good sample size, bablock regression method may lead to same results as obtained from other methods. So, more authentic research methods are required for good analysts.[8] Bruegel M et al., suggested that the Bland-Altman method is more advantageous as it is a graphical analysis which produces more authentic results. Even extreme results of different parameters can be exhibited in this analysis.[9] Therefore, we also used the Bland-Altman method to validate the consistency of results by instruments used for comparison. In this study, the Bland-Altman analysis showed that results of swelab and sysmex are within 95% of consistency limit. It is observed that the results of both analysers are comparable, and the two intruments are reliable.

The difference between the two instruments was statistically significant as p value was <0.5. Out of 100 samples, 10 patients were having platelet count <150,000/µl and these were further verified by manual method. Another study done by Anitha k et al., suggested that manual method of platelet count on peripheral smear, is more economic, fast and

authentic diagnostic tool which can be performed in any laboratory even with and without availability of modern and new equipments.[10]

CONCLUSION

A good correlation of parameters of complete blood count was obtained by Swelab Alfa Plus standard and sysmex xp-100 analyzers. Results of these instruments are consistent and precise so they can be placed and used in any laboratory.

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CLINICAL PRESENTATION AND SURGICAL PROCEDURES IN PATIENTS WITH COLORECTAL CARCINOMA

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Abstract

Objective: To find out the common presentation, staging and surgical procedures in Patients with Colorectal Carcinoma (CRC). It was a cross sectional study conducted in the Department of Surgery, Avicenna Medical College/ Hospital Lahore, from January 2015 to December 2019.

Methodology: A total of 92 patients diagnosed as CRC were included in the Study. The Parameters analyzed were Age, Gender, mode of presentation, location of Primary Tumor, Surgical procedures performed and stage of the Tumor. Duke's staging was done with the help of CT Scan of Abdomen/Pelvis/Chest, Operative findings and histopathological reports.

Results: A total of 92 patients were included during the study period 52 (56.52%), patients ware male and 40 (43.47%) females. The Age range was 20 to 70 years of age. The most common site of the CRC was Rectum 40(43.47%) and most common Clinical presentation was bleeding per Rectum 68 (73.91%). A large no of patients with CRC treated by Abdomino-perineal Resection 40 (43.47%), and 42 (34.78%) patients presented in Duke's stage D.

Conclusions: CRC is male predominance disease. The most common site of CRC is the Rectum while the Bleeding per Rectum remains the most common Clinical presentation.

Keywords: Colorectal Carcinoma, Duke's staging, Rectum.

Colorectal Carcinoma (CRC) also known as Large Bowel Cancer includes Cancerous growth of Colon Rectum and Appendix. CRC, is the major cause of morbidity and mortality all over the world.[1] CRC is the second commonest cause of cancer related death in both males and females in developed countries.[2] The incidence is higher in men than women. CRC incidence is higher in hereditary conditions like Familial Adenomatous Polyposis and Hereditary Non-Polyposis colorectal coli.[3]

Right and Left sided colon cancers affect the prognosis and treatment1 of the disease. Left sided tumors are located in the distal 1/3 of Transverse colon, Splenic Flexure, Descending colon, sigmoid colon and Rectum. Right sided tumors are present in the Appendix, Caecum, Ascending colon, Hepatic Flexure and proximal 2/3 of the Transverse colon, Left sided CRC is more common than Right sided CRC.[4]

There is great variability in clinical presentation. The commonest and earlier is the Bleeding per Rectum.[5] The patients of CRC may require emergency surgical procedure. Duke's grading is helpful for the management of CRC pts. CRC used to occur in young and old age, however during recent decades, younger patients are being seen. The treatment of CRC is the surgery, whether curative or palliative depending upon the stage of the disease. Prognosis of CRC is also related to the stage of disease at presentation.[6]

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This study has been conducted to find out the clinical presentation, Anatomical location of the tumor and surgical procedures under taken.[7]

METHODOLOGY

This was cross sectional study, conducted in Department of Surgery in Avicenna Medical College/ Hospital Lahore from January 2015 to December 2019. All patients with Biopsy proven CRC admitted during the period diagnosed as having CRC, were included in this study. The Parameters analyzed were, Age, Gender, mode of presentation, location of the primary tumor, surgical procedure performed and staging of the tumor.

All patients underwent colonoscopy and Biopsy, along with CTS Scan of Abdomen/ Pelvis and other baseline investigations including, Blood complete picture, Liver function Tests (LFT) serum Proteins, viral and tumor Markers, the patients latter on had planned surgery, followed by adjuvant Chemo therapy/ Radio therapy. The patients presented as Intestinal Obstruction had emergency surgery and the resected specimen had histopathological examination. Cancer having site proximal to Distal 1/3 of Transverse colon, were grouped as Right sided while any cancer in the Rectum, Sigmoid colon, Descending colon, Splenic flexure distal 1/3 of the Transverse colon were defined as left sided cancer. Duke's classification was employed for the staging of tumors.

RESULTS

A total of 92 patients with CRC diagnosed were included over the study period. There were 52(56.52%) male and 40(43.47%)females. The Age range was 20 to 70 years. There were 50(54.34%) between 20 to 40 years, 40(43.47%) between 40 to 60 years and 2 (2.17%) above 60 years of age these 92 patients 52(56.52%) were admitted via OPD and 48(52.17%) through Emergency room. The most common presentation was bleeding per rectum. Table–I. n = 68 (73.91%). Anatomically most common involved site was rectum, 40(43.47%). In 52 (56.52%) patients tumor involved other parts of colon. Table-III. Stage D was more common n = 42 (45.65%) Table-II. The distribution according to Duke's Table-II classification was Stage A4(4.34%), Stage B 9(9.78%), Stage C 37(40.21%), Stage D 42(45.65%). Different Surgical procedures done included Right Hemi colon 60(65.21 %), APR 40(43.47%) Anterior Resection 30(32.60%), Hart's man procedure 3(3.26%), and left hemi colectomy in 13(40.625%).Table-IV

Table 1: *Common presentation of colorectal carcinoma*

Clinical presentation	Number (n)	Parentage
Bleeding Per Rectum	**68**	**73.91**
Constipation	**8**	**8.69**
Altered Bowel Habits	**9**	**9.78**
Abdominal Pain	**7**	**7.60**

Table 2: *Duke's stage of colorectal carcinoma*

Stage of Colorectal carcinoma	Number	Percentage
Stage A	4	4.34
Stage B	9	9.78
Stage C	37	40.21
Stage D	42	45.65

Table 4: *Surgical Procedures*

Procedure	Number (N)	Percentage
Abdominal Perianal Resection (APR)	40	43.47
Anterior Resection	30	32.60
Right Hemi Colectomy	6	6.521
Left Hemi Colectomy	13	14.13
Hartman's Procedure	3	3.26

DISCUSSION

The risk factors which predispose for the Causation of CRC is usually, positive family history along with diet, smoking and inflammatory Bowel Diseases[2].

CRC is primarily a disease of the elderly butt its

Table 3: *Sites of Colorectal Carcinoma*

Site	Number (N)	Percentage	Site	Number (N)	Percentage
Appendix	0	0	Transverse colon Distal 1/3	3	3.26
Caecum	0	0	Splenic flexure	0	0
Ascending colon	3	3.26	Descending colon	9	9.78
Hepatic flexure	0	0	Sigmoid colon	34	36.95
Transverse colon Proximal 2/3	3	3.26	Rectum	40	43.47

incidence in young age group is increasing.[8] It is generally assumed that due to a predominant Vegetarian diet, people in the devolving countries have a low incidence of CRC.

Unfortunately, In Pakistan CRC[3] screening is not done due to higher literacy rate and unawareness of its importance.[19] The patients with CRC[4] is diagnosed very much late. This point also reflected in our study. In which not a single case was diagnosed by screening Colonoscopy[17]. The prognosis is worse when the disease occurs in the young adults due to advanced stage of the presentation and delayed diagnosis[18].

The common Gut parts involved were Rectum and Sigmoid colon[20]. The young patients had more advanced disease at the time of first presentation.[12] The common presentation of CRC is Bleeding per Rectum. Early diagnosis is important to have better prognosis.[13]

Colonoscopy is the most accurate and widely used method for screening CRC.[14]

Emphasis is also done in follow up for the detection of metastatic disease.[15,16]

CONCLUSION

Most of the CRC patients present in the 3rd and 4th decade of life with male predominance. The common clinical presentation c CRC was bleeding per rectum. Left sided colon was predominantly involved and most common side was Rectum.

More frequent Endoscope Evaluation may be able for early diagnosis / treatment of CRC patients.

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SURGICAL APPROACH FOR MANAGING DIFFERENTIATED AND MEDULLARY THYROID CARCINOMAS

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Abstract

Objective: To determine the frequency and surgical management of Papillary, Follicular and Medullary Carcinoma of Thyroid gland. It was a retrospective study conducted at the department of surgery Avicenna Medical College/ Hospital Lahore, from March 2016 to June 2020.

Methodology: All patients with Well Differentiated Thyroid carcinoma and medullary thyroid carcinoma were included in the study. The patients of anaplastic tumor and malignant lymphoma thyroid were excluded. Written consent about the surgical procedure and complications was taken.

Results: Two hundred Patients were included in this study 134(67%) were female and 66(33%) were male. The most frequently Thyroid carcinoma was the Papillary carcinoma encountered in 140(70%). Various surgical procedureswere performed to manage these Thyroid carcinomas. Total Thyroidectomy was preferred operation for Differentiated Thyroid carcinoma. Total Thyroidectomy was done in 186(84%) patients. For Medullary carcinoma surgical procedure done was Total Thyroidectomy with Bilateral Block Neck dissection.

Conclusions: The most common thyroid carcinoma is the papillary carcinoma followed by follicular carcinoma. The medullary carcinoma which originates from para-follicular cells of thyroid carcinoma is rare.

Keywords: Papillary carcinoma, follicular carcinoma, medullary carcinoma

Papillary and Follicular Carcinomas are from Follicular cells while Medullary Carcinoma is derived from Para-Follicular cells of Thyroid gland.[1] Papillary and Follicular are referred to be Differentiated Thyroid Carcinoma.

Thyroid Carcinoma is the most common Endocrine Tumor.[2] The incidence of Well Differentiated and Medullary carcinoma has increased with the passage of time. The Papillary Thyroid Carcinoma is the commonest Thyroid Tumor.[3]

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These Thyroid Tumors usually present as solitary thyroid nodule, multinodular goiter and enlarged thyroid gland with cervical lymphadenopathy. Fine Needle Cytology (FNAC) has important and well-established role in clinical solitary nodule, but limited role in the multinodular goiter[4] (MNG). Various surgical procedures are being done for the management of these Thyroid Tumors.[5] This study was done to know the frequency, the clinical presentation and management of Papillary/Follicular carcinoma (Differentiated) and Medullary carcinoma of Thyroid gland.[6]

METHODOLOGY

This was retrospective study. This study was done in Avicenna Medical College/Hospital Lahore, March 2016 to June 2020. The patients of Differentiated carcinomas (papillary, follicular) and medullary carcinoma were included in the study.

All patients with thyroid disease were examined and different Radiological & Histological Investiga-

tions were done. Ultrasonography and CT scan of neck were done to know the Retro-sternal extension and invasion of Carotid vessels, Esophagus and tracheas by the tumor and cervical lymph node status, FNAC was also done. The diagnosis of Thyroid carcinoma was done on FNAC finding or Histopathological reports of excised cervical lymph nodes or Thyroid tissues. The drain was kept in huge thyroid gland, Havingtotal thyroidectomy and in the Neck dissection. Each patient was checked for bleeding from the wound/drain and sings/Symptoms of hypocalcemia in the post-operative period in the ward. In follow up period the thyroid hormone replacement therapy was advised in patients with total thyroidectomy. Further treatment was planned according to the histopathological reports and on Oncologist advice.

RESULTS

Two Hundred patients were included in this study. Out of these 134(67%) were Female and 66(33%) were Male, with female to male ratio of 2:1. Papillary carcinoma was the most frequently thyroid carcinoma encountered n=140, (70%).

Table 1: Incidence of Thyroid Carcinoma

Thyroid carcinoma	N	%
Papillary carcinoma	140	70
Follicular carcinoma	46	23
Medullary carcinoma	14	7
Total patients	200	

Table 2: Complications in Thyroid Surgery

Complications	Total Thyroidectomy N=180 (90%)	Total Thyroidectomy with Bilateral Block Neck Dissection 14(7%)
Temporary Voice Change	2(1%)	1(0.5%)
Permanent Voice Change	0%	0%
Transnet Hypocalcaemia	3(1.5%)	1(0.5%)
Permanent Hypocalcaemia	0%	0%
Wound Infection	4(2%)	1(0.5%)
Seroma Formation	6(3%)	2(1%)

Follicular carcinoma was found in 46 (23%) patients and Medullary carcinoma in 14 (7%) patients was detected in Table I. Total Thyroidectomy was preferred and procedure of choice in the patients diagnosed as Papillary and Follicular Thyroid carcinomas. Total Thyroidectomy was done in 186 (93%) patients. Medullary carcinoma was managed by total Thyroidectomy with Bilateral Block Neck dissection and this procedure was on 14 (7%) patients. Various complications recorded during these surgical procedures are shown in Table II.

DISCUSSION

The extent of the surgical resection in the Well Differentiated Thyroid Carcinoma has remained controversial. However, the total thyroidectomy is preferred than unilateral lobectomy.[8]

Total Thyroidectomy is the procedure of choice in pts with tumor size more than 4cm, multifocal disease, bilateral disease, Clinical or Radiological involvement of cervical lymph nodes and distant metastasis.[9,10] Total thyroidectomy for WDTC helps in the detection and ablation of metastatic disease with Radioactive iodine.[11,12] The incidence of Thyroid carcinoma is steadily rising in the world. Treatment of medullary carcinoma is the total thyroidectomy with Bilateral Block Neck dissection.[13,14]

CONCLUSION

Papillary and follicular carcinoma which are also called differential thyroid carcinomas arise from Follicular cells while medullary carcinoma is derived from para-follicular cells of thyroid gland. Papillary carcinoma of thyroid is the commonest malignancy with female predominance. Papillary and follicular tumors are usually found in patients of 3rd and 4th decade of life. Total thyroidectomy is procedure of choice for differentiated thyroid carcinoma while medullary thyroid carcinoma is treated by total thyroidectomy along with bilateral block neck dissection.

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SURGICAL MANAGEMENT OF PHYLLODES TUMOR OF BREAST

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Abstract

Objective: To evaluate the different surgical procedures and Post-operative recurrence in patients with phyllodes Tumor of Breast. It was a retrospective study conducted in the department of Surgery, Rahbar Medical & Dental College/ Hospital Lahore from January 2016 to March 2019.

Methodology: Twenty eight diagnosed patients of phyllodes tumor were admitted through OPD. The patients categorized into benign, borderline and malignant. Surgical procedure was performed after pre-operative assessment follow up of these patients was done in surgical OPD.

Results: Out of 28 female patients, 16 (57.14%) patients were Benign, 5 (17.85%) Borderline and 7(25%) were of Malignant disease. The most commonly affected site was upper/outer Quadrant of the breast. Surgical procedure performed were wide local Excision with one cm clear margins in 21(75%) and simple mastectomy in 7(25%) There was no motility.

Conclusion: Wide local excision with one cm clear margins is preferred over simple mastectomy in patients desiring for Breast conserving surgery. Adjuvant Chemotherapy further reduces the risk of all local and systemic recurrence rates.

Keywords: Breast tumor, phyllodes tumor, wide local excision

The phyllodes tumors also known as cystosarcoma phyllodes are rare fibro epithelial tumors of female breast. They tend to re-occur locally and metastasize through blood.[1] This study determines the recent experience in diagnosis of phyllodes tumors. phyllodes Tumor follows an unpredictable course. It has got the ability to re-occur locally and also ability to metastasize.[2] They are commonly found between 35 years to 55 years of age. They may be Benign, Borderline and Malignant. Although distant metastases are uncommon but can occur through blood stream to lungs and bones. Lymphatic spread is rare. Benign as well as Malignant tumors have propensity to re-occur.[3] The diagnosis of phyllodes tumor is made by Clinical examination imaging, FNAC and histopathological. Report Tumor markers are very little informative. The primary surgical treatment is wide local Excision with more than one cm clear margins. Recurrent, malignant and large massive tumors need simple mastectomy.[4] Postoperative Radio therapy is advised to prevent re-occurrence and improve the disease free survival in malignant patients. This study was done to evaluate the surgical treatment options and post-operative recurrence.[5]

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METHODOLOGY

This reterospective study was done in the department of surgery Rahbar Medical College / Hospital Lahore from January 2016 to March 2019. 28 patients were included in this study. Diagnosis was made by Triple Assessment i.e. Clinical Examination (History and Examination) imaging (ultra sound, Mammo-

graphy) and pathology (FNAC) and Biopsy. The phyllodes tumors were graded into Benign, Borderline and Malignant by using WHO classification. The patients with malignant disease were investigated further for distant metastasis. All patients were investigated and assessed for fitness for general Anesthesia. The patients underwent either wide local Excision with one cm clear margins or simple mastectomy. Post-operative patients were monitored in the ward. The patients with malignant disease were advised adjuvant chemotherapy. Follow up of the patients was done in surgical OPD. Parameters like age, parity; site and size of tumors, surgical procedure, histopathological report and post-operative outcome were recorded.

RESULTS

Twenty eight patients were managed from January 2016 to March 2019. Their ages were from 20 – 55 years with a mean age of 47.5 years. In benign cases, the tumor size was 5 cm or less in 10 patients and more than 5 cm in 8 cases. In Borderline, the tumor size was more than 5 cm. The borderline patients were 5(17.85%)in malignant cases, which were 7(25%) had tumor size more than 5 cm. Right breast was involved in 16(75.14%) patients and left breast in 12(42.85%) patients. The upper /outer quadrant of breast was involved in 20(71.42%) patients. According to histological report, 16(57.14%) patients had benign disease. 5, had Borderline and 7 had malignant disease. The surgical procedure performed wide local excision with adequate clear margins in 21(75%), patients and simple mastectomy in 7(25%), patients. During follow up period, 3(10.71%), patients of benign disease, 2(7.14%), patients of Borderline and I patient with malignant disease developed recurrent disease. Recurrent Benign and Borderline patients underwent simple Mastectomy and Postoperative Adjuvant Chemotherapy. Recurrent malignant patient was advised adjuvant Chemotherapy.

Table 1: *Histopathological Report and Procedure Performed*

Histopathology	Wide Local Excision	Simple Mastectomy
Benign n= 16(57.14%)	15(53.28%)	1(3.57%)
Borderline n= 5(17.85%)	4(14.28%)	1(3.57%)
Malignant n=7(25%)	2(7.28%)	5(17.85%)

Table 2: *Follow up and recurrence*

No. of Patients	Complete Follow Up	Incomplete Follow Up	Recurrence
Benign N=16(57.14%)	14(50%)	2(7.14%)	3(10.71%)
Borderline n= 5(17.85%)	4(14.28%)	1(3.57%)	2(7.14%)
Malignant n=7(25%)	5(17.85%)	2(7.14%)	1(3.57%)

DISCUSSION

Phyllodes tumor of the breast are rare, fibro-epithelial tumors.[6] phyllodes tumors patients have variable malignant potential Metastasis has been reported in small percentage of cases. Phyllodes tumor tend to re-occur locally.[7] The management of patient presented to surgeon with unique challenges. Majority of these tumors are managed by with wide local excision with 1 cm clear margins or by simple mastectomy. The patients often present with painless lump in the breast. Most communally lump is located in the upper and outer quadrant of breast.[8] They vary greatly in size. Right side of the breast is usually more involved and moreover nulliparous women are more involved.[9] The phyllodes tumors may be benign, borderline and malignant. Surgery is mainstay of the primary treatment of patients. The aim should be to excise the lesion with adequate clear margins to prevent re-occurrence.[10] Simple mastectomy is recommended in malignant patients. For borderlines lesions the optimal primary treatment is controversial. Simple mastectomy for malignant and borderlines tumors had better results than breast conserving surgery.[12] Follow up of patients is mandatory as because benign as well as malignant lesions can re-occur, locally and metastasize distally.[13] The re-occurrence rate of patients is variable. In malignant patients postoperative adequate chemotherapy is recommended to decrease the re-occurrence and improve the disease free survival.[14]

CONCLUSION

Phyllodes tumor bears specific clinical characteristics and can be considered as differential diagnosis of Breast lumps. The pre-operative diagnosis and proper management are crucial in phyllodes tumors because of their tendency to re-occur and malignant

potential in some of these tumors.

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SURGICAL MANAGEMENT OF RETERO-STERNAL GOITER

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Abstract

Objective: This study aims to evaluate surgical approaches for the management of patients with retro-sternal goiter. It was a retrospective study, conducted at Avicenna Medical College/Hospital Lahore from January 2009 to November 2019.

Methodology: Thirty two patients were admitted through outdoor patient's department. CT scan was done in all patients to know the extent of Retro-sternal Goiter. Patients with recurrent Thyroid surgery were excluded.

Results: This study included 32 patients of retro-sternal goiter. Out of which 22 (68.75%) were female and 10 (31.25%) were Male. Male to Female ratio was (2:1). Age of these patients was from 40-62 years. 30(93.75%) managed by Collar Neck incision while 2(6.25%) patients needed midline sternotomy. There was no mortality.

Conclusion: The Expert Surgeon can manage the retrosternal goiter by Neck Collar incision with minimal complications.

Keywords: Retro-sternal goiter, sternotomy

Retro-sternal goiter is defined as a Thyroid mass that extends 3 or more centimeters below.[1] The supra-sternal notch when the neck is Hyper extended. RSG can occur in 1-20% of Goiters. RSG are usually benign in nature although an underlying neoplastic process may be found.[2] The patients with RSG remain as sympathetic for a long time; have the potential for sudden enlargement secondary to hemorrhage, Cystic degeneration or malignant change which can be life threatening.[3] Surgical removal is the gold standard curative treatment which prevents potentially fatal compressive symptoms. There are several surgical approaches such as collar incision, sternotomy and thoracotomy.[4] The aim of this study was to evaluate the Presentation and Surgical management of the Patients with retro-sternal goiter.[5]

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METHODOLOGY

This Retrospective study was conducted at Avicenna Medical College/Hospital Lahore from January 2009 to November 2019.All 32 patients included in this study were clinically evaluated in surgical OPD. Written informed consent was taken. All 32 patients who were included in this study underwent total thyroidectomy. Recurrent Laryngeal nerve and Parathyroid glands were identified and saved in all patients. In difficult cases midline sternotomy was done. Hypocalcemia and other Thyroid surgery complications evaluated. All patients were discharged with thyroid hormone replacement therapy.

RESULTS

A total of 32 patients were included in this study. There were 22(68.75%) female and 10 (31.25%) male patients. The Female to Male ratio was 2:1. Age of the patients was from 40-62 years. The most

common presentation was Neck swelling that was present in 30 Patients. Two patients had cough/dyspnea but no neck swelling was observed. These two patients were diagnosed with the help of investigations 24 (75%) patients presented with difficulty in breathing. 30 (93.75%) had retro-sternal extension in anterior mediastinum where as 2 (6.25%) patients had retro-sternal extension in posterior mediastinum.30 (93.75%) patients were managed through cervical Collar incision where as 2 (6.25%) needed a midline sternotomy. The surgical procedure done was total thyroidectomy. Histopathological reports showed Multi Nodular Goiter with no malignancy in the gland. There was no operative modality. All 32 patients were followed up Post operatively. All patients received thyroid-hormone replacement therapy for the rest of life.

DISCUSSION

RSG was 1st discovered by Haller 1749. RSG predominantly found in female patients.[6] RSG is typically slow growing in nature. RSG is usually contained in anterior mediastinum.[7] The main complaint caused by RSG is breathing difficulties and clinical diagnosis can be hindered by the lack of an anterior neck mass.[8] The presence of an RSG is an indication for surgery owing to lack of medical treatment, the high incidence of symptoms related to compression.[11] Low surgical morbidity/motility and risk of malignancy.[9,10] Surgical management for patients with RSG requires careful pre-operative planning and many factors should be taken into the account when considering alternative approaches such as sternotomy and thoracotomy.[12,13]

Surgery is more commonly performed via Cervical Collar incision with mandatory availability additional sternotomy.[14,15]

CONCLUSION

As chance of complication is very much high in the retro-sternal goiter surgery. It is a great challenge to the surgeons for surgical management of retro-sternal goiter. Majority of retro-sternal patients can be managed by Neck incision, midline sternotomy with minimal complications.

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SYNOVIAL SARCOMA OF THYROID GLAND, A RARE CASE

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Abstract

Synovial sarcoma is a variant of soft tissue sarcoma with preponderance to involve extremities. We are reporting a case of primary synovial sarcoma of thyroid which is a rare occurrence. A 22 years old female underwent total thyroidectomy during pregnancy. Morphology, immunohistochemistry and presence of t(X; 18) all favored diagnosis of synovial sarcoma. Patient deferred treatment for 6 months due to childbirth and presented later on with recurrent neck mass with cervical lymphadenopathy. Now she is being treated at our institution with multidisciplinary approach. Early diagnosis and treatment is crucial in management of this aggressive disease.

Key Words: synovial sarcoma, thyroid gland, t (X; 18)

Sarcomas account for 1% of all malignancies.[1] Synovial sarcoma is most common soft tissue sarcoma in adolescent and young adults after rhabdomyosarcoma, which is clinically, morphologically and histologically distinct from other subtypes of soft tissue sarcoma.[2] Monophasic and biphasic are two main histological subtypes of it.[3] Majority of cases involve para articular region of extremities with 10% cases occurring in head and neck region[(4)]. Synovial sarcoma arising from thyroid gland is extremely rare with only a few cases reported in literature. When a malignancy arises in an unusual site, it not only makes its diagnosis difficult, treatment also becomes a challenge. Here we report a case of primary synovial sarcoma of thyroid gland in a pregnant lady, with early recurrence after surgery.

CASE REPORT

A 22 years old female presented during 2nd trimester of her pregnancy with complaint of swelling in front of her neck for last 15 months that had rapidly increased in size over last 2 months causing occasional difficulty in swallowing. Previously she had no significant medical, surgical or family history related to thyroid disease. She was advised routine investigation along with thyroid function tests which came out to be within normal range. Her ultrasound neck showed 25×23.2mm heterogeneous mass in Right lobe of thyroid gland. Fine needle aspiration cytology was performed in which presence of groups and sheets of atypical spindle cells with hyper chromatic nuclei and some nuclear and cellular pleomorphism was seen, which favored spindle cell neoplasm

Her MRI neck was performed that showed well defined oval shaped mass measuring 3.4×3.2×6.2cm arising from right lobe of thyroid lying deep to sternocleidomastoid muscle, postero-laterally abutting ipsilateral common carotid and internal jugular vessels, medially mass was abutting thyroid cartilage. Multiple cervical lymph nodes were seen at bilateral level II and III largest measuring 13×20mm at right level II.

Taking into consideration rapidly progressing and aggressive nature of disease her urgent total thyroidectomy along with selective cervical lymph node dissection was performed by taking high risk consent during 6th month of her pregnancy.

On gross examination, 6×4×2cm nodule was seen arising from isthmus which was well circumscribed with solid white firm cut surface. Microscopic features revealed a circumscribed highly cellular

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neoplasm comprising spindle cells arranged in fascicles, sheets and herring bone pattern showing nuclear pleomorphism and occasional mitotic activity, while lymph nodes showed reactive hyperplasia only.

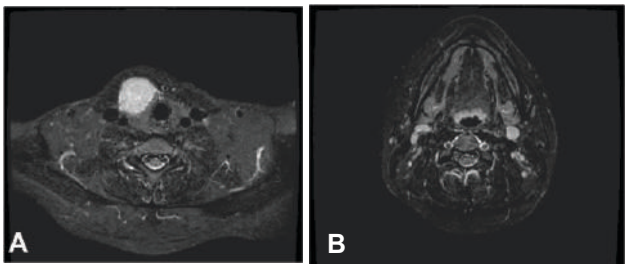

Figure 1.

1A: TIWI axial images showing oval shape mass isointense to muscle and arising from right lobe of thyroid.

1B: T2 STIR axial section showing multiple bilateral cervical lymph nodes.

The biopsy specimen was sent for review which confirmed above mentioned findings. On immunohistochemistry, neoplastic cells stained with EMA, TLE1 and S100 which supported diagnosis of synovial sarcoma, monophasic type.

Diagnosis was further confirmed by detection of SS18 gene rearrangement by FISH assay using dual color, break part rearrangement probe.

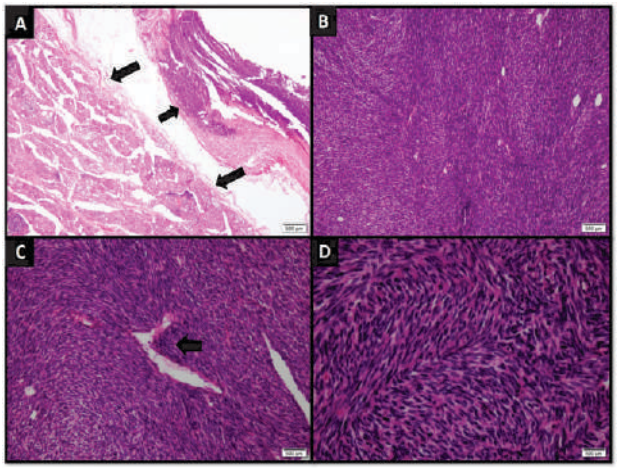

Figure 2. *[A] Low power view of tumor surrounded by fibrous pseudocapsule (small arrow) and adjacent benign thyroid gland (larger arrows) [B] Tumor cells arranged in parallel fascicles [C] Hemangiopericytoma-like blood vessels (arrow)* ***[D]*** *Tumor cells have elongated, vesicular nuclei which do not exhibit significant pleomorphism and mitotic activity*

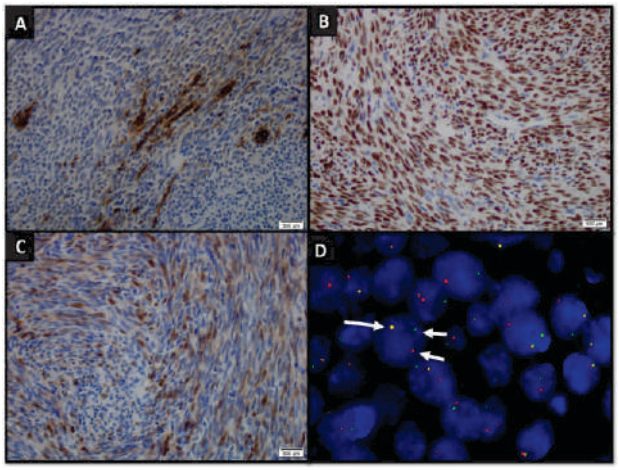

Figure 3. *Tumor cells demonstrate positive expression for [A] EMA, [B] TLE1 and [C] S100 IHC stains. FISH analysis shows SS18 gene translocation resulting in red and green signals (short arrows). Normal gene shows yellow signal (larger arrow).*

Unfortunately, patient lost to follow up and presented 6 months after thyroidectomy with recurrent disease in neck. At this time, 0.8×0.7cm enhancing soft tissue nodule was appreciable in pre-tracheal region at level of C5 with multiple enlarged bilateral level I, II, III, IV lymph nodes on CT scan neck and chest with contrast. Patient is now being treated at our hospital by multidisciplinary approach involving general surgeon, medical oncologist and radiation oncologist.

DISCUSSION

Sarcomas account for 1% of all malignant cancers, of which 10% are bone sarcomas while majority cases are of soft tissue in origin.[1] Incidence of soft tissue sarcoma is 2-3/100,000 people. Synovial sarcoma is a type of soft tissue sarcoma which is seen in both pediatric and adult patients with peak incidence seen in 3rd decade of life. It differs from other types of sarcomas in clinical presentation, morphology and genetics. t(X;18) which leads to fusion of SYT gene on chromosome 18 with SSX1, SSX2 or SSX3 gene on X chromosome is characteristically seen in these patients.[2] Monophasic and biphasic are two main histological subtypes of synovial sarcoma. In monophasic form spindle cells are seen under

microscope with epithelial differentiation evidenced only on immunohistochemistry while in biphasic form, glandular or solid epithelial structures are usually clearly visible. Myxoid, hemangiopericytic, calcifying, ossifying and poorly differentiated are important morphological patterns of synovial sarcoma. On immunohistochemistry, these tumors are CK+, EMA+, bcl2+, S100+/-, CD99+/-[3] Owing to pro-pensity of local invasiveness and distant metastasis it should always be considered as high-grade sarcoma.[(2)] Commonly, these tumors arise from para-articular regions of extremities with 10% cases being seen in head and neck region. Normal synovial cavity is not stained with epithelial markers, so synovial sarcoma is not related to normal synovium, but arises from pluripotent mesenchymal cells which are capable of epithelial differentiation. Synovial sarcoma arising from thyroid gland is a rare entity and it may arise from mesenchymal cells of capsule or stromal tissue of thyroid.[4] In literature, only few cases of synovial sarcoma of thyroid are present. In 2003, KiKuchi I, reported case of a 65 years old patient who presented with complaint of hoarseness of voice, with 6.8×6.5cm mass which on histopathology showed presence of spindle cells and presence of t(X,18).[5] In 2007, case of a 15 years old boy with biphasic synovial sarcoma was reported in Journal Of Korean Medical Sciences who presented with palpable neck mass.[4] Similar cases were reported in literature in 2001, 2003, 2014 and 2017.[6,7,8,9]

In our case, a young female had a thyroid swelling in front of her neck for 15 months that increased in size during her pregnancy. Initially it was thought to be pregnancy related change, hence only thyroid function tests were advised which were within normal range. But as size was increasingly rapidly further investigations including neck ultrasound, FNAC and later on MRI neck plain were advised. Contrast studies like thyroid scan, CT scan with contrast were avoided. Considering the presence of atypical malignancy in thyroid alarmed treating surgeon, hence, her urgent total thyroidectomy along with selective lymph node dissection was performed after explaining condition and taking high risk consent. Patient was referred to oncologist who confirmed the diagnosis by reviewing histopathology specimen along with detection of specific chromosomal translocation t(X, 18) which is specific for synovial sarcoma. Patient lost to follow up for 6 months, as she underwent caesarian section for child birth which led to delay in receiving treatment. Her CT scan neck and chest with contrast was advised to look for current status of disease that not only showed local recurrence of disease but also presence of enlarged cervical lymph nodes. Now her treatment is ongoing at our institution and she is responding very well.

When a malignancy occurs in an unusual location, it is a difficult task not only to diagnose it but also treat it as we don't know how will it behave and respond to recommended treatment options.

Patient's Consent

Informed consent was taken from the patient for publication of this case.

Conflict of Interest

Authors declared no conflict of interest.

Authors' Contribution

SY: Drafted initial manuscript

SY, AK, AZ, AG: Diagnosed and managed the case, reviewed and finished the work.

MT, AR: Diagnosis of case

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