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Editorial

Original Articles

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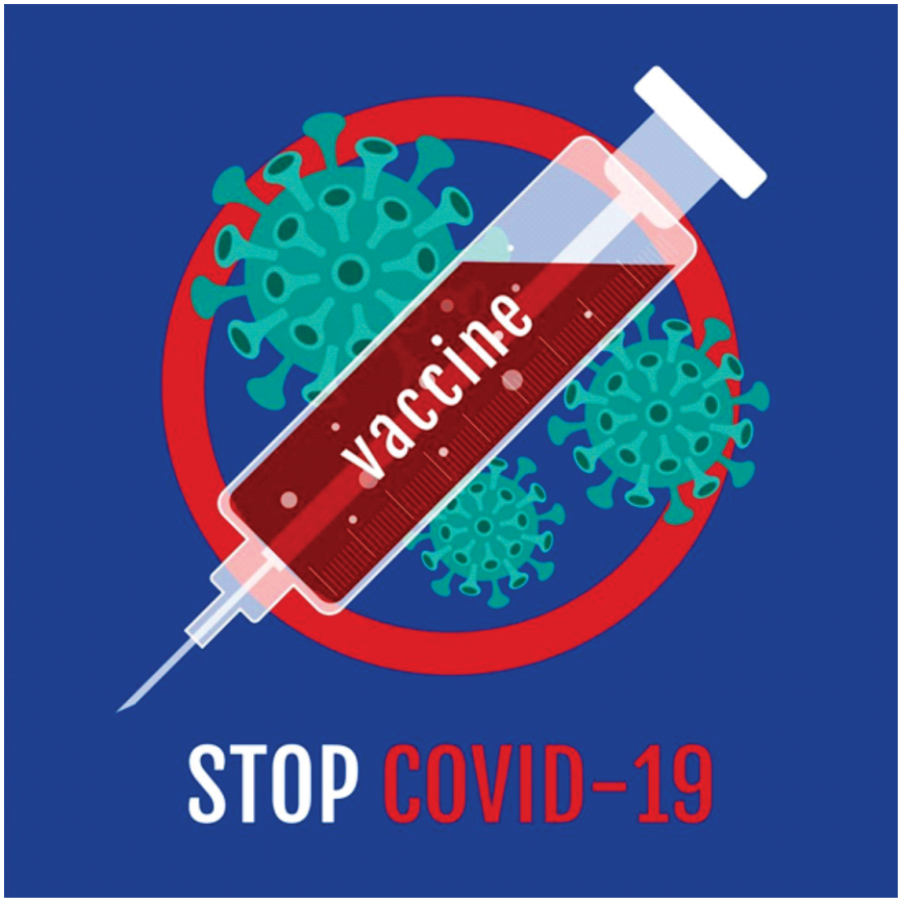

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THE RACE FOR COVID-19 VACCINE

A vaccine is a biological preparation that provides active acquired immunity to an infectious disease. A vaccine contains an agent that resembles a disease-causing microorganism and is often made from weakened or killed forms of the pathogen, its toxins, or one of its surface antigenic proteins. Vaccination is one of the most effective ways to prevent certain diseases**.** A vaccine helps the body's immune system to recognize and fight micro-organisms like viruses and bacteria, which then keeps the individual safe from the diseases they cause. Vaccines can both be prophylactic, to prevent or ameliorate the effects of a future infection by a particular pathogen, or can be therapeutic, e.g., vaccines against cancer, which are still under investigation. Vaccines protect against more than 25 debilitating or life-threatening diseases, including measles, polio, tetanus, diphtheria, meningitis, influenza, tetanus, typhoid and even cervical cancer. Thanks to vaccines that helped bring some of the deadly diseases under control.

For millennia, small pox was one of the world's most feared diseases, killing 30% of the patients and leaving survivors, scarred and blind. In 1796, Edward Jenner developed a vaccine. Immunizing people with a cowpox vaccine created immunity to small pox. Small pox was finally eradicated in 1970s. In 1918, Spanish flu outbreak affected one third of the world population. 500 million people were affected and 50 million were killed. It was caused by a virus thought to be coming from birds, H_1N_1. A vaccine introduced in 1945 prevented millions of deaths. Whooping cough, tetanus, diphtheria can lead to serious illness and death. In 1948 first combination vaccine for these three diseases was introduced, but some adverse affects were seen, so a new inoculation was developed in the 1900, which is still in use. Polio is a debilitating disease, which attacks the central nervous system. Jonas Salk, in 1955 prepared a vaccine which helped bring polio under control and a decade later oral vaccine was introduced by Sabin. Polio is eradicated from the entire world leaving Nigeria, Afghanistan and our own homeland Pakistan with the disease. Prompt measures are needed at all levels in the country to bring this crippling disease under control. Ebola is one of the most deadly diseases known in the recent past. A major outbreak in 2014 in Guinea, West Africa led to successful human trails of a vaccine, making a major breakthrough in the fight against this killer virus.

Unlike most of the drugs, whose benefits are restricted to the individual who take the drug, vaccines given as prophylaxis, have the potential for far-reaching effects, that encompass: health services utilization, general well being and health, cognitive development, ultimately and economic productivity. The impact of immunization is measured by evaluating effects of the vaccine directly on the individual, indirectly on the unvaccinated community; known as herd immunity, the epidemiology of the pathogen; such as changing circulating serotypes of the micro-organism or prevention of epidemic cycles, and the additional benefits which arises from improved health. Apart from protection of the individuals, the broader success of vaccination is dependent on achieving a level of coverage sufficient to interrupt the transmission of the micro-organism. When evaluating the cost-effectiveness of a vaccine, all of the above mentioned potential benefits need to be taken into account.

Dozens of teams around the world are racing to form a vaccine for COVID-19. A striking feature of the vaccine development for COVID-19 is the range of technology platforms being evaluated, including nucleic acid (DNA and RNA), virus-like particle, peptide, replicating and non-replicating viral vectors, recombinant protein, live attenuated virus and inactivated virus approaches. Many of these techniques are not currently the basis for licensed vaccines, but experience in some other fields like oncology is encouraging the developers to exploit the opportunities that next-generation approaches offer for increased speed of development and manufacture. It is conceivable that some vaccine platforms may be better suited to a specific population subtypes, such as the elderly, children, pregnant females or immune-suppressed patients

The devastating scale of the humanitarian and economic impact of the COVID-19 pandemic is driving evaluation of next-generation vaccine technology platforms through novel techniques to accelerate the development; however experts say having a vaccine ready within 18 months would be very fast.

References: W.H.O.

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Hope is being able to see that there is light despite all of the darkness.
Photograph: ***Ali Rizvi***

PREVALENCE OF GASTRIC VARICES, THEIR TYPES AND ASSOCIATIONS AMONG LIVER CIRRHOSIS PATIENTS

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Abstract

Objective: To determine the prevalence of gastric varices, their types and associations in patients suffering Liver cirrhosis who underwent upper gastrointestinal endoscopy (UGIE) at Liver Clinic, Lahore, Pakistan.

Study Design: Retrospective cohort study

Methodology: In a retrospective analysis of patients who underwent UGIE from July 2010 to June 2014, presence gastric varices, types of gastric varices, gender, age groups, grade of esophageal varices (EV), presence of portal hypertension gastropathy (PHG), gastric vascular ectasia (GVE), and hiatal hernia + reflux esophagitis (HH+RE) were the qualitative variables, while age of the patients was a quantitative variable. The data was evaluated on SPSS version 25, where means and standard deviations were calculated for quantitative variable, and frequencies and percentages were computed for qualitative variables. The bivariate analysis was performed to determine the significant relation of different predictive factors with presence of gastric varices. While applying chi-square test of independence, a p value of equal to or less than 0.05 was considered as significant. The odds ratio along with their 95% confidence interval (CI) were also calculated for each association.

Results: Out of the total of 2463 chronic liver disease (CLD) patients who underwent UGIE, 64.4% were male and 35.4% were female. Their mean age was 51.03 + 10.18 years, and the mean weight was 72.70 + 15.55 Kilogram. The prevalence of fundal varices was 12.4% (n=305); amongst which 22.6% (n=69) had GOV1, 13.1% (n=40) had GOV2, 58% (n=177) had IGV1, 1% (n=3) had IGV2, 0.7% (n=2) had GOV1 along with GOV2, and 4.3% (n=13) had GOV2 along with IGV1. 12.5% males and 12.2% females had fundal varices. Similarly, in different age groups, 0% adolescents, 11.8% young adults, 12.2% middle aged adults and 16.1% older adults had fundal varices. The association of finding fundal varices with gender (p=0.898), different age groups (p=0.456) was not statistically significant. 12.6% patients without EV, while 10.2% with grade I EV, 12.6% with grade II EV and 15.1% with grade III EV had fundal varices. Amongst the patients with PHG, 12.8% had fundal varices, while amongst the patients without PHG, only 4.9% had fundal varices. Similarly, amongst the CLD patients without GVE, 12.9% (n=289) had fundal varices, and 7.1% (n=16) patients with GVE had fundal varices. 12.9% CLD patients without HH+RE had fundal varices, while only 0.9% (n=1) patients with HH+RE had fundal varices. The occurrence of fundal varices had a statistically significant association with different grades of esophageal varices (p=0.023), presence of PHG (p=0.007), absence of GVE (p=0.011), and absence of HH+RE (p=0.000).

Conclusion: Gastric varices were prevalent in liver cirrhosis patients, amongst which IGV1 were the most common in our population. GV were more prevalent in association with grade III EV as compared to grade I and II EV. However, their prevalence in different age groups and gender had no statistical significance. Presence of GV in liver cirrhosis patients may have a protective or inhibitory role for the development of HH+RE and GVE.

Keywords: Gastric varices, Sarin Categories, Retrospective analysis, statistical associations

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Gastric varices (GV)[1] are dilated submucosal veins that occurs secondary to portal hypertension or splenic vein obstruction.[2] Sarin classified GV into 4 types.[3] Gastroesophageal varices (GOV) type 1 and GOV type 2 are the esophageal varices that extend below cardia into stomach along lesser curvature and greater curvature respectively. Isolated gastric varices (IGV) type 1 and IGV type 2 are in the fundus and elsewhere in the stomach respectively. The prevalence of GV in cirrhosis is estimated to be 15-17%.[3,4,5] GOV1 are more frequent approximately 75%, and IGV2 are extremely infrequent among all GV. GV have a lower risk of bleeding than EV. However, their bleeding tends to be more severe with a higher mortality, approximately 45%.[3]

Left gastric vein, a branch of portal vein, is involved in the formation of EV and GOV1. The branches of splenic vein in posterosuperior part of the gastric wall, short gastric vein and posterior gastric vein, are involved in the formation of GOV2 and IGV1. Some branches of splenic vein and superior mesenteric vein are responsible for IGV2.6 GV are drained by portosystemic collaterals. EV and GOV1 drains via azygous veins, while IGV1 drains via left inferior phrenic vein (IPV) into left renal vein or inferior vena cava. GOV2 drains via both EV and IPV.[7]

GOV1 share the vascular anatomy as that of EV, so treatment plan for both is same. Primary prophylaxis includes non-selective beta blockers (NSBB) for high risk small EV/GOV1 (with red sign or in CTP-C patient), and NSBB or carvedilol, or endoscopic variceal band ligation (EVBL) for medium or large EV/GOV1. Secondary prophylaxis includes combination of NSBB and EVBL (1st line) and TIPS (2nd line). For GOV2 or IGV1, primary prophylaxis includes NSBB while secondary prophylaxis includes TIPS or BRTO. Similarly, for actively bleeding GOV2 or IGV1, TIPS is the treatment of choice. Cyanoacrylate glue injection is an option if TIPS or BRTO are not technically feasible in secondary prophylaxis or actively bleeding GOV2 or IGV1.[8,9,10] Dual venous connection makes the management of GOV 2 difficult. BRTO eradicates its posterior (fundal) part drained by IPV, and may remain its anteromedial (cardiac) part which is drained by esophageal varices. This part may need transhepatic embolization or EVBL.[11]

When we see gastric varices in liver cirrhosis patients, additional endoscopic findings like esophageal varices (EV), portal hypertension gastropathy (PHG), gastric vascular ectasia (GVE), and hiatal hernia + reflux esophagitis (HH+RE) are also found. The available international data is scarce about any association of gastric varices with these additional findings.

The objective of this study was to find the prevalence of gastric varices, their types and associations in patients suffering Liver cirrhosis who underwent upper gastrointestinal endoscopy (UGIE) at Liver Clinic, Lahore, Pakistan.

METHODOLOGY

This was a retrospective cohort study carried out at Liver clinic, 250 Shadman Lahore. Amongst the CLD patients who underwent UGIE from July 2010 to June 2014, the patients with gastric varices were evaluated. GV were divided into 4 types according to Sarin classification.[3] The esophageal varices extending below the cardia into stomach along lesser curvature and greater curvature were named as GOV1 and GOV2 respectively, while isolated gastric varices are in the fundus and elsewhere in the stomach were named as IGV1 and IGV2 respectively. The age of the patients was categorized into childhood if < 13 years, adolescence if 13-18 years, young adults if 19-44years, middle aged adults if 45-65 years, and older adults if >65 years.[12,13]

EV were graded from I to III as follow: small and straight EV were Grade I, EV, tortuous varices occupying <1/3 of the esophageal lumen were grade II, and larger occupying >1/3 of the esophageal lumen were grade III EV.[14]

The presence gastric varices, types of gastric varices, gender, age groups, grade of esophageal disease, presence of portal hypertension gastropathy,

GVE, and HH+RE were the qualitative variables, while age of the patients was a quantitative variable. The entire data was evaluated on SPSS version 25. During descriptive interpretation of data, means and standard deviations were calculated for the presentation of quantitative variable, and frequencies and percentages were computed for qualitative variables. The bivariate analysis was performed to determine the significant relation of different predictive factors with presence of gastric varices. While applying chi-square test of independence, a p value of equal to or less than 0.05 was considered as significant. Moreover, odds ratio along with their 95% confidence interval (CI) were also calculated for each association.

RESULTS

A total of 2463 chronic liver disease (CLD) patients underwent UGIE, out of which 1587 (64.4 %) were male and 876 (35.4%) were female. Their mean age was 51.03 + 10.18 years with a range of 14 to 95 years, while their mean weight was 72.70 + 15.55 Kilogram with a range of 29-131 kilogram. 305 (12.4%) patients had fundal varices; amongst which 22.6% (n=69) had GOV1, 13.1% (n=40) had GOV2, 58% (n=177) had IGV1, 1% (n=3) had IGV2, 0.7% (n=2) had GOV1 along with GOV2, and 4.3% (n=13) had GOV2 along with IGV1. (Picture 1-3)

Amongst the CLD patients who underwent UGIE, 12.5% males and 12.2% females had fundal varices. The association of finding fundal varices with gender was not statistically significant (p= 0.898). Amongst the CLD patients who underwent UGIE, 0% adolescents, 11.8% young adults, 12.2% middle aged adults and 16.1% older adults had fundal varices. The association of occurrence of fundal varices in different age groups was also not statistically significant (p=0.456). 12.6% (n=22) CLD patients without esophageal varices, while 10.2% (n=100) CLD patients with grade I esophageal varices, 12.6% (n=68) with grade II esophageal varices and 15.1% (n=115) with grade III esophageal varices had fundal varices. The occurrence of fundal varices had a statistically significant association with different grades of esophageal

Table 1: *Correlation of Presence of Gastric Varices with different Parameters (n = 305/2463)*

Parameters /Categories	Gastric varices		Total	p-value	Odd ratio with 95% Confidence interval
	Yes	No			
Gender:					
Male	198 (12.5%)	1389 (87.5%)	1587	0.898	1.024 (0.797-1.317)
Female	107 (12.2%)	769 (97.8%)	876		
Age groups:					
Adolescent	0 (0%)	3 (100%)	3	0.456	*
Young Adults	68 (11.8%)	506 (88.2%)	574		
Middle aged adults	212 (12.2%)	1519 (87.8%)	1731		
Older adults	25 (16.1%)	130 (83.9%)	155		
Grade of Esophageal varices:					
No	22 (12.6%)	152 (87.4%)	174	0.023	*
Grade I	100 (10.2%)	885 (89.8%)	985		
Grade II	68 (12.6%)	472 (87.4%)	540		
Grade III	115 (15.1%)	649 (84.9%)	764		
Portal hypertensive gastropathy:					
Yes	299 (12.8%)	2042 (87.2%)	2341	0.007	2.831 (1.235-6.489)
No	6 (4.9%)	116 (95.1%)	122		
Gastric vascular ectasia:					
Yes	16 (7.1%)	210 (92.9%)	226	0.011	0.514 (0.304-0.867)
No	289 (12.9%)	1948 (87.1%)	2237		
Hiatal hernia ± Reflux esophagitis:					
Yes	1 (0.9%)	105 (99.1%)	106	0.000	0.064 (0.009-0.463)
No	304 (12.9%)	2053 (87.1%)	2357		

* Odd ratio can only be computed for 2 × 2 tables

varices (p=0.023) Amongst the patients with PHG, 12.8% (n=299) had fundal varices, while amongst the patients without PHG, only 4.9% (n=6) had fundal varices. The occurrence of fundal varices in CLD patients with portal hypertensive gastropathy had statistically significant association (p=0.007). Similarly, amongst the CLD patients without GVE, 12.9% (n=289) had fundal varices, while only 7.1% (n=16) CLD patients with GVE had fundal varices. The association of occurrence of fundal varices in CLD patients without GVE was statistically significant (p=0.011). 12.9% (n=304) CLD patients without hiatal hernia + reflux esophagitis had fundal varices, while only 0.9% (n=1) CLD patients with hiatal hernia + reflux esophagitis had fundal varices. The association of occurrence of fundal varices in CLD patients without hiatal hernia + reflux esophagitis was statistically significant (p=0.000).

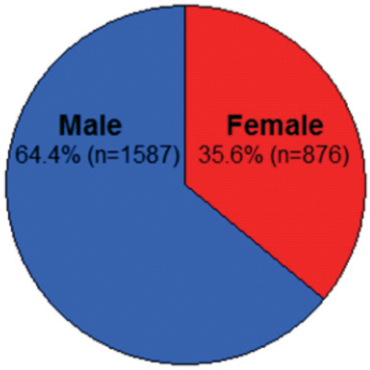


Fig. 1: *Gender Wide Distribution of Fundal Varices*

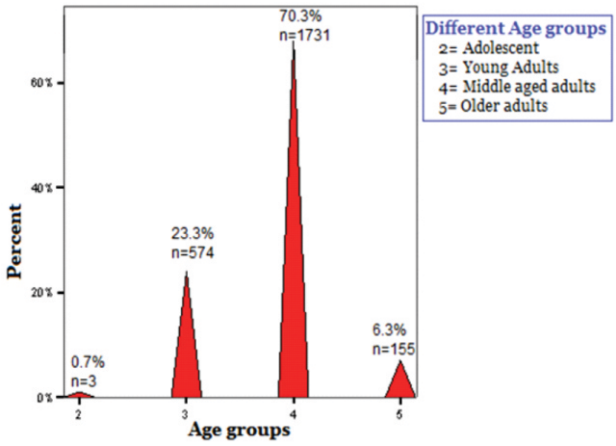
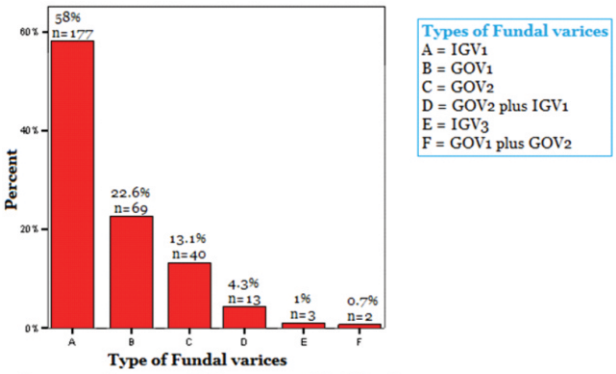


Fig. 2: *Distribution of Fundal Varices in Different Age Groups.*



Picture 3: Frequency of different types of Fundal varices

Fig. 3: *Frequency of Different Types of Fundal Varices*

DISCUSSION

Gastric variceal bleed is a serious complication in decompensated liver cirrhosis and the endoscopist should be familial of its different types, their location, and management. Type of GV (IGV1> GOV2> GOV1), large size, presence of red sign, and severity of liver dysfunction are the factors associated with higher risk of bleeding. [15]

In a study, Mudawi, Ali and Tahir found 16.8% prevalence of GV. Similarly, in 2007, Khalid Mumtaz and his colleagues reported the prevalence of GV of 15% (220/1436) in portal hypertension patients in Karachi. In our study of 2463 CLD patients, the prevalence of GV was 12.4%. Perhaps, the prevalence of GV in liver cirrhosis patients of our population was decreasing. This hypothesis requires further studies to validate these findings.

In 1992, Sarin and colleagues reported that amongst GV, GOV1 were the most common (75%) while IGV2 were extremely infrequent. In our study, IGV1 were most prevalent (58%) followed by GOV1 (22.6%). IGV2 were least prevalent (0.7%). This prevalence variation may be due to difference in distribution of portal hypertension in our population.

Mudawi and colleagues also noted that GV were more prevalent in patients with grade I and grade II EV. However, reverse was found in our data. The prevalence of GV was 10.2%, 12.6%, and 15/1 % in patients with grade I, II, and III EV respectively.

Whether, gastric varices have protective role in

the development of HH + RE in cirrhotic patients. International data is scarce on this hypothesis. In our data, 0.32% (1 out of 305) cirrhotic patients with gastric varices had HH + RE, while 4.8% (105 out of 2158) cirrhotic patients without gastric varices had HH + RE. In past, multiple studies showed high prevalence of GERD in liver cirrhosis patients.[16] No one study correlated Hiatal hernia in cirrhosis patients with gastric varices. Our observation of less prevalence of HH + RE in conjunction with gastric varices may point the protective role of gastric varices in occurrence of HH + RE in cirrhotic patients. This hypothesis may require further studies to be validated. In our study, 5.2% (16 out of 305) cirrhotic patients with gastric varices had GVE while 9.7% (210 out of 2158) cirrhotic patients without gastric varices had GVE. Perhaps, development of gastric varices in cirrhotic patients has an inhibitory effect on development of GVE. No reference evidence was found in literature discussing this effect. I think, further larger studies are required to validate these findings.

CONCLUSION

Gastric varices are prevalent in liver cirrhosis patients, amongst which IGV1 are the most common in our population. The GV are more prevalent in association with grade III EV as compared to grade I and II EV. However, their prevalence in different age groups and gender has no statistical significance. The occurrence of gastric varices in liver cirrhosis patients had a protective or inhibitory role for the development of HH+RE and GVE.

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BASELINE CD4$^+$ T CELL COUNT IN HIV INFECTED, TREATMENT NAIVE PATIENTS REFERRED TO TERTIARY CARE CENTRE

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Abstract

Background & objectives: HIV (Human immunodeficiency virus) results in acquired immunodeficiency syndrome (AIDS) by causing destruction of CD4$^+$ T cells. CD4$^+$ count assesses the severity of immune suppression in HIV infected individuals. It plays a vital role in staging the disease, when to start treatment, monitoring disease course and to determine treatment failure. This study was conducted to assess baseline CD4$^+$ count at initial presentation of ART(antiretroviral therapy) naive HIV-positive subjects.

Methodology: It was descriptive cross sectional study. A sum of 106 treatment naive subjects of HIV infection with all genders and age range of 18-65 years were enrolled. Blood samples were taken and base line CD4$^+$ lymphocyte count evaluated on flowcytometer which carries out cell sorting and analysis. Data was analyzed in software SPSS 23.

Results: Mean age of patients present in this study was 31.4 ± 8.5 (18 -65 years). Out of the total 106, fifty eight (57.4%) belonged to age group 18-29 year. Eighty three (78.3%) were males, 17 (16%) were female patients and 6 (5.7%) were trans-gender. Male to female ratio was 4.8:1. Thirty eight (35. 8%) patients had CD4$^+$ count of ≤350 cells/mm^3, while 68 (64.2%) had above 350 cells/mm^3. Seven patients (6.6%) had CD4$^+$ count ≤50 /µL, whereas 10.4% had between 51-200 /µL, and 18.9% had CD4+ count in range of 201-350/µl.

Conclusion: In our study about half of the HIV subjects fall in category of normal baseline CD4$^+$ count. Initially CD4$^+$ count was the principal measure to decide when to start treatment, but now it should be initiated irrespective of baseline CD4$^+$ count. Investigating CD4$^+$ count distribution in ART-naive HIV positive person still has strong inference for management.

Key Word: Human immuno deficiency virus, Acquired immune deficiency syndrome , CD4$^+$ Counts

Cd4$^+$ 'cluster of differentiation' is a glycoprotein on the surface of helper T cells, macrophages, dendritic cells and monocytes. In humans, the CD4$^+$ protein is encoded by the CD4$^+$ gene.[1] T lymphocytes are categorized as (1) T Helper cells is a main regulator of immune system.[2] (2) T Cytotoxic cells kills virus infected cells.[3] (3) T Suppressor cells down regulates the function of T helper cells and cytotoxic T cells.[4]

HIV (Human immunodeficiency virus) results in acquired immunodeficiency syndrome (AIDS) by causing destruction of CD4$^+$ T cells.[5] CD4$^+$ count assesses the severity of immune suppression in HIV infected individuals. There is reciprocal relationship between CD4$^+$ T cell count and severity of immuno-suppression.[6] The reference methods utilized for monitoring HIV infection are flowcytometric analysis and PCR which provide the CD4$^+$ T cell count and plasma viral load. There are few laboratories in resource limited countries which carry out these

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tests.[7] It plays vital role in staging the disease, making decision when to initiate treatment, monitoring disease progression and treatment failure. Generally, $CD4^+$ count has advantage over viral load as both test are very expansive to carry out at a time.[8] $CD4^+$ count determination is comparatively cheaper and affordable in under developed countries.[6] $CD4^+$ counts are expressed as the number of cells per µl (or mm,^{3} cubic millimeter^3) of blood, with reference range of 500-1200 cells/mm.^{3} HIV-infected individual with < 200 cells per micro liter is labeled as AIDS.[1] The lowering of $CD4^+$ T helper cells deteriorates the immune system and allows opportunistic infections.[9]

Globally there are 34 million HIV infected people as reported by United Nations HIV&AIDS Programme (UNAIDS), out of which about 23.5 million are living in sub-Saharan Africa.[10] By the end of 2011, globally 14.8 million HIV infected individuals are treatment eligible, eight million are taking antiretroviral treatment in low- and middle-income countries.[11] There were 2.5 million new infections and 1.7 million deaths due to HIV/AIDS in 2011.[12] HIV/AIDS is diagnosed by laboratory tests and staging is based on certain signs and symptoms.[13] WHO (World Health Organization) staging system is more popular in under developed countries while CDC (Centers for Disease Control) classification system is more frequently utilized in developed world. The WHO staging relies more on clinical picture than $CD4^+$ count because $CD4^+$ count tests may not be available in resource limited countries. While, CDC's classification system uses $CD4^+$ T cell count to stage HIV infection.[14] This system was developed and updated in 2008, HIV infections are classified according to $CD4^+$ count. 1st stage: CD4+ count ≥ 500 cells/microlitre. 2nd stage: CD4+ count 200-499 cells/microlitre. 3rd stage: CD4+ count < 200 cells/microlitre. Accordingly AIDS is defined as all HIV-infected patients with CD4+ count <200 cells/ microlitre or $CD4^+$ cell percentage is <14%.[15]

A study conducted in Islamabad in 2015 showed that mean $CD4^+$ count was 434.30±269.23, with minimum $CD4^+$ count of 9.00, and maximum of 1974 cells /microlitre but it did not mention the proportion of subjects according to CDC classification categories.[16]

In another study in Lahore revealed that Twenty two (35.5%) cases had a $CD4^+$ count more than 455 /µl while forty patients (64.5%) had a count of less than 455 /µl.[17]

Initially, it was recommended that ART should be initiated when CD4+ < 200 cells/mm^3, the criteria changed to <350 cells/mm^3 in 2008. In 2013, the recommendation to initiate ART at $CD4^+$ counts <500/mm^3 was documented while currently, it is recommended ART should be started immediately with the informed consent if HIV infection was determined.[18]

According to updated WHO guidelines ART should be started in all HIV-infected adults regardless of $CD4^+$ count or WHO stage. There is increased patient benefit when routinely ART is initiated at $CD4^+$ counts greater than 500 cells per microliter.[19]

Very few studies in Pakistan have looked at baseline $CD4^+$ counts trends at the time of registration in to HIV care and initiation of treatment under the HIV program in Pakistan. This study was conducted to assess the $CD4^+$ count on first presentation of ART naive HIV-infected subjects attending the department of Pathology Allama Iqbal Medical College Lahore.

METHODOLOGY

It was descriptive-cross-sectional study conducted in Pathology department at Allama Iqbal Medical College, Lahore during Jan 2016 to June 2016. A total of 106 newly diagnosed treatment naive, subjects of HIV infection with all genders and age range between18-65 (years) were enrolled in the current study through non-probability purposive sampling referred from Punjab AIDS Control Programme (PACP). This study was approved by the Ethical Review board Allama Iqbal Medical College. In accordance with the Helsinki Declaration, all patients enrolled in the study com-

pleted a written informed consent form. Excluding all those taking antiretroviral therapy, self reporting patients and patients having documented evidence co-morbidity with other medical conditions (e.g. tuberculosis, endocarditis, congenital immune disorder and acute viral infections) that could significantly modify hematologic parameters.

Responses about sociodemographic factors like age, sex, marriage and income etc were entered in pre designed structured proforma.

Five ml of venous blood samples were taken from every patient in EDTA vacutainer tubes between 09:00 am and 12:00 pm and analyzed within 6 hours. CD-4 lymphocyte count were evaluated on BD FACS Calibur, "an automated four colour" flowcytometer which performs both cell sorting and analysis. The counts were determined by a monoclonal antibody cocktail comprised of $CD3^+$ PerCp, $CD4^+$ FITC and $CD8^+$ PE in a TruCount tube.

Data was analyzed in software SPSS 23. Frequencies, percentages, mean and SD (standard deviation) were calculated. Cross tabulations were carried out.

RESULTS

The data was presented from total of 106 patients after complete documentation and necessary study requirements. Mean age of subjects included in the study was 31.4 ± 8.5 with the range of 18 and 65 years. Fifty eight (57.4%) of the total subjects in this study were in age group of 18-29 year, 32(30.2%) in the age group of 30-39 years, 10(9.4%) were in age group of 40-49 years and 6 (5.7%) were of age ≥50 years. Sixty five (61.3%) of the study population was married and 41(38.7%) unmarried cases (Table 3.1). Out of the 106 subjects there were 83 (78.3%) males, 17 (16%) female patients and 6 (5.7%) trans-gender(Figure No1). Male to female ratio was 4.8:1 (Table No 1). In terms of income 40(48.8%) were having income slab of Rs; 5001-10000, details of the rest are given in (Table No1).

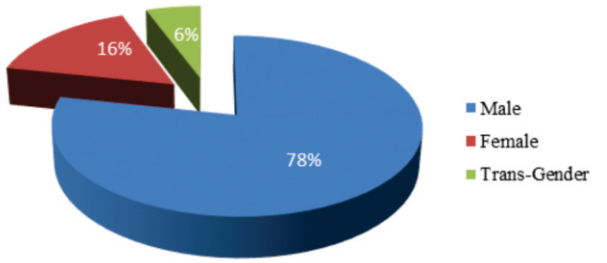

Figure. 1: *Gender Distribution of HIV patients*

Table 1: *Socio-Demographic Features of (n=106), HIV/AIDS Patients*

	Parameter	Frequency	Percent
Age (Groups)	18-29	58	54.7%
	30-39	32	30.2%
	40-49	10	9.4%
	⩾50	6	5.7%
	Total	106	100.0%
Gender (Groups)	Male	83	78.3%
	Female	17	16.0%
	Trans-Gender	6	5.7%
	Total	106	100.0%
Marital Status	Married	65	61.3%
	Single	41	38.7%
	Total	106	100.0%
Income (Groups)	Rs: ⩽5000	23	28.0%
	Rs: 5001-10000	40	48.8%
	Rs: 10001-30000	17	20.7%
	Rs: 30001-50000	1	1.2%
	Rs: >50001	1	1.2%
	Total	82	100.0%

In terms of occupation, 24 patients (22.6%) were labourers, 13.2% were house wives, 6.6% were drivers, 6.6% were shopkeepers, 5.7% were unemployed, 4.7% were dancers and lastly 27.3% were having other professions. (Table No 2).

Seven patients (6.6%) were having $CD4^+$ count of ≤ 50 cells/microlitre, 10.4% between 51-200 cells/microlitere, and 18.9% observed $CD4^+$ count 201-350 cells/microlitre. Those having $CD4^+$ count between 351-500 cells/microlitre were 18 (17%), 14.2% had between 501-600 cells/mm^3, 20.8% had between 601-800 and lastly 12 patients (13.2%) had $CD4^+$ count of above 800 cells/mm^3. Thirty eight (35.8%) patients had $CD4^+$ count of ≤ 350 cells/mm^3,

while 68 (64.2%) had above 350 cells/mm^3. (Fig No 2 Table No 3.

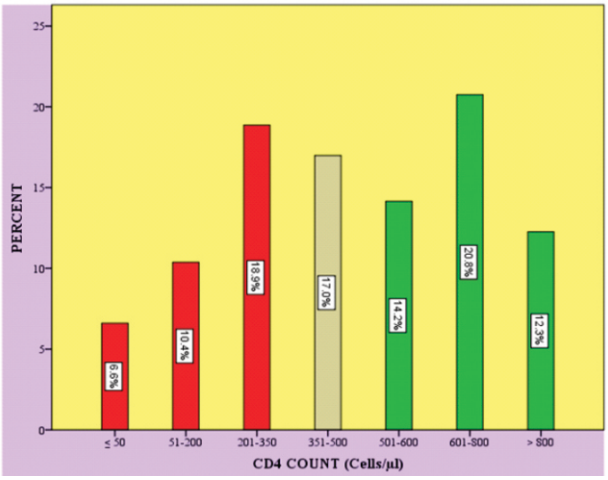

Figure 2: *Shows CD4+ Cell Count of HIV Positive*

Table 2: *Distribution of occupations in HIV/AIDS patients*

PROFESSION	FREQUENCY	PERCNT
LABOURER	24	22.6
HOUSE WIFE	14	13.2
DRIVER	7	6.6
SHOPKEEPER	7	6.6
JOBLESS	6	5.7
DANCER	5	4.7
SALE MAN	5	4.7
STUDENT	4	3.8
TAILOR	4	3.8
SEX WORKER	1	0.9
OTHERS	29	27.3
TOTAL	106	100

Table 3: *Distribution of CD4+ counts in HIV/AIDS patients*

CD4+ Cell Count	Frequency	Percent	Cumulative Percent
⩽ 50	7	6.6	6.6
51-200	11	10.4	17.0
201-350	20	18.9	35.8
351-500	18	17.0	52.8
501-600	15	14.2	67.0
601-800	22	20.8	87.7
> 800	13	12.3	100.0
Total	106	100.0	

Patients (n= 106)

DISCUSSION

WHO suggests antiretroviral therapy to all youngsters, adults and expecting women with CD4+ count <350 cells/µl or those with symptoms nevertheless of CD4+ count.[20] Accordingly, high percentage of our study patients (35.8%) would need antiretroviral treatment having CD4+ count < 350 cells/µl. In a study from Africa, the overall percentage of people with CD4+ count below the eligibility thresholds for treatment of 200 and 350 cells /µl was 4.2% and 13.5%, respectively.[21] Starting treatment at this stage minimize the death risk.[22] Additional benefits of treatment also include a less risk of progression to AIDS, improve physical and mental health,[23-24] a decrease in transmission risk among sexual partners and less mother to child transmission.[25] However, it is important to note that people with severe and advanced clinical conditions (Clinical stage 3 & 4 by WHO) should commence ART regardless of the number of CD4+ cells.[1]

In this study, 68 (64.2%) people had CD4+ cell count of more than 350 cells/µl and 18.9% had CD4+ count 201-350 cells/µl. Those who had 351-500 cells/µl were 18(17%), 14.2% had between 501-600 cells/mm^3, 20.8% had between 601-800 and lastly CD4+ count of above 800 cells/mm^3 was seen in (13.2%) cases. In a study conducted in Africa 27.2 % and 25.3% of HIV ART naive cases were having Cd4+ count between 201-350 and 351-500 cells/mm^3 respectively.[26]

There appears to be a consensus on ART deferral in HIV asymptomatic patients whose CD4+ count is more than 500 cells /µl.[1,27] These HIV patients would require counseling advice and follow-up. After the widespread use of strong antiretroviral regimens, the incidence of previous widespread opportunistic infections and even cancers decreased significantly, and mortality dropped proportionally. Untreatable infections, requiring lifelong maintenance, no longer require treatment after antiretroviral treatment.[1]

Male:female ratio in the current present study

(4.8:1) is comparable but much higher than 1.2:1 of Oguejiofor et al., 2008.[28] However, HIV prevalence declined among young women aged 15–24 years in the past 12 years in both urban and rural populations.[29] Thus, discrepancy in gender occurrence is age-dependent. The current study evaluated only those who were enrolled for $CD4^+$ counts, therefore, it did not explore between males and females who are more prone to get HIV infection. However, females may be more prone to get HIV due to early marriages, polygamous relationships and PID (pelvic inflammatory disease).[30-31]

In our study the majority of the affected people were in reproductive age group i.e. 18-29 and 30-39 years, can be ascribed to the reality that these age segments are sexually active, more prone to unprotected sex, drug abuse and acts related to young-looking excitement. This raises the economic load and affects the in general progress of the family, community and the nation. Also in a study conducted by Kumawat S et al., the majority of the affected people were from low to middle socio economic class and reproductive age segment of 15-44 years.[32]

The 40-49 years and ≥ 50 age segments had the lowest number of HIV infected subjects: 10(9.4%) and 6 (5.7%) respectively. HIV/AIDS is linked with reduction in life expectancy but if treatment is started early after the diagnosis of AIDS, then life expectancy is about 10-40 years.[20,33]

Labour was generally a common occupation seen to be affected in our study. In a similar study commonest occupation group was labour followed by skilled/self-employed workers.[32]

The frequency of patients with CD4+ count ≤ 200 cells/µl in our study was 18 (17%), according to CDC classification, they may be suffering from AIDS. A similar community based study revealed 13.6% of the cases having $CD4^+$ count ≤ 200 cells/µl in ART naive HIV patients.[22] Contrary to this in Ethiopia about two third (64.4%) of the patients were found to have base line $CD4^+$ cell counts ≤ 200 cells/µl.[34] Following the diagnosis, if treatment is not initiated in AIDS, survival is in few months.[35-36] The principal causes of mortality from HIV infection and AIDS are opportunistic infections and cancer that frequently result from progressive immune destruction.[37]

This study mainly focuses on a center based data (PACP), which appears to be a drawback. The $CD4^+$ count ranges would certainly vary if all HIV-positive individuals in communities were examined and analyzed. This is well recognizable fact that many HIV-infected people are ignorant about their virus infection. This data of the study reflected only the people who voluntarily visited the referral center in Lahore. Voluntary counseling and testing is an important way to enhance access to diagnosis and treatment. Moreover, early diagnosis will help to identify patients with a higher number of $CD4^+$ cells, thus improving prognosis.

CONCLUSION

In our study about half of the HIV subjects fall in category of normal baseline $CD4^+$ count. Studies on the distribution of baseline $CD4^+$ count in previously untreated HIV infected patients have a strong management effect. The decision, when to start antiretroviral therapy was initially related to the level of immuno-suppression and disease progression, assessed by the number of $CD4^+$ cells. Now worldwide WHO recommendations are being adopted, so antiretroviral therapy should be commenced regardless of baseline $CD4^+$ count. It is imperative for clinicians to be vigilant about risk of treatment cessation among HIV-infected individuals with high baseline $CD4^+$ counts.

Recommendations

Few studies have been carried out on baseline $CD4^+$ count distribution on our population in Pakistan. Further extensive research is required on a larger scale on this aspect.

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Health is not valued till sickness comes

Thomas Fuller

ACCURACY OF HIGH-RESOLUTION COMPUTED TOMOGRAPHY CHEST IN DETECTION OF SPUTUM SMEAR-NEGATIVE PULMONARY TUBERCULOSIS AND FORMULATING A PREDICTABILITY CRITERIA KEEPING GENE XPERT AS GOLD STANDARD

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Abstract

Objectives: To study the accuracy of high-resolution computed tomography (HRCT) chest in the diagnosis of pulmonary tuberculosis (PTB) in sputum smear negative patients, confirmed with gene Xpert MTB/RIF test and to design HRCT criterion to predict the diagnosis of pulmonary tuberculosis.

Methods: We conducted a retrospective cohort study which included 138 patients who were twice sputum smear negative for acid-fast bacilli (AFB) but had strong clinical suspicion of PTB. All of them underwent HRCT chest followed by gene Xpert test. Their histories, risk factors, co-morbid factors and HRCT-results were evaluated. At the end of our study we formulated an HRCT diagnostic criteria in view of the outcomes.

Results: Amongst the clinical presenting complaints, chronic cough, low grade fever and night sweats were linked to a greater risk for developing PTB. HRCT findings of cavitation, centrilobular nodules, tree in bud configuration, consolidation, interlobular septal thickening, pleural effusion, main lesion in S1, S2, S6 and lymph adenoapthy were main imaging findings. Our HRCT indicative criteria demonstrated reliable sensitivity and specificity for PTB patients determining that HRCT is a useful tool in sputum negative PTB patients.

Conclusion: HRCT Chest is highly efficacious in predicting risk of PTB in the sputum smear-negative setting even when gene Xpert test is not available.

Keywords: Tuberculosis pulmonary, computed tomography, smear -negative sputum

Pulmonary tuberculosis (PTB) is a common worldwide infection and a medical and social problem causing high mortality and morbidity, especially in developing countries.[1] PTB is caused by Mycobacterium tuberculosis. Other species can cause similar disease, including Mycobacterium bovis, Mycobacterium africanum, Mycobacterium microti, and Mycobacterium canettii. It's an airborne infection, transmitted by droplets 1–5µm in diameter, which can remain suspended in the air for several hours when a person with active tuberculosis coughs, sneezes, or speaks. It's important to note that not all individuals exposed to tuberculosis get infected. Instead the probability being infected depends on the infectiousness of the tuberculosis source, the environment and duration of exposure, and the immune status of the exposed individual.[2] Once the droplets reach the terminal airspaces by means of inhalation, they infect the alveolar macrophages. Only in approximately 5% of infected individuals, the immune system is inadequate at controlling the initial infection, and primary active

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tuberculosis develops within the first 1–2 years. In another 5% of infected individuals, the immune system is effective at controlling the initial infection, but viable mycobacteria remain dormant and reactivate at a later time manifesting as postprimary or reactivation tuberculosis. The remaining 90% of the exposed individuals will never develop symptomatic disease but harbor the bacterium as latent tuberculosis with no risk of contamination.[3]

Active disease can present as primary or postprimary tuberculosis, shortly after being infected or developing after a long period of latent infection. Primary tuberculosis is most commonly found in children and immunocompromised patients, who present with lymphadenopathy, consolidation anywhere in the lung and pleural effusion. Postprimary tuberculosis presents with cavitations, apical consolidations, tree in bud and centrilobular nodules.[4] PTB can also present as military nodularity in cases of hematogenous spread.[4] The lab investigations of testing for active tuberculosis are sputum analysis, including smear, culture, and nucleic acid amplification, gene Xpert MTB/RIF, pleural tap, CXR, HRCT chest.[5] If TB is detected early and fully treated, people with the disease quickly become noninfectious and eventually cured. However, multidrug-resistant (MDR) and extensively drug-resistant TB, HIV-associated TB, and weak health systems are major challenges.[6] Hence, familiarity with the imaging, clinical, and laboratory features of tuberculosis is important for prompt diagnosis and management.

Acid-fast bacilli are found in the sputum in a limited number of patients with active PTB.[7] Therefore, the imaging diagnosis can predict the presence of disease in infected patients before the definitive diagnosis by bacteriology. The aim of this article is to review the characteristic imaging findings of PTB, and to assess the role of HRCT in the early diagnosis of PTB in smear negative patients keeping gene xpert as gold standard and to formulate an HRCT criteria to establish early diagnosis of PTB.

METHODOLOGY

In this retrospective study, the data of 138 patients with HRCT prediction of PTB was collected over a period of one year from January 2018 to January 2019. Histories were assorted and it was found that majority of the patients presented with persistent cough of at least 2 weeks or more, hemoptysis, weight loss, fever, or night sweating. All patients were twice sputum smear negative for acid fast bacilli (AFB). All sputum samples had been sent for direct smear examination using Zeihl-Neelsen Stain in the same pathology lab. Patients who were sputum smear positive, pediatric patients and patients with only extra-pulmonary involvement were excluded. HRCT chest had been conducted using 64 slice Philips machine at Jinnah hospital, Lahore.

Statistical Analysis

Data was evaluated with SPSS statistical software version 20. A standard deviation with $p< 0.05$ shows a significant relationship. Positive predictive values, negative predictive values, sensitivity and specificity were designed wherever relevant.

RESULTS

Age of the participants varied between 14 to 80 in this study. Average age was 38.5 years. 76 were men and 62 were women.102 patients were found to have PTB. Remaining 36 patients had other disease. Among the clinical variables, chronic cough, fever, weight loss and night sweats were significantly linked with greater chance of having PTB. (Table 1)

HRCT Findings

Table 1: *Clinical Findings of PTB & Non-PTB Patients*

	PTB	Non-PTB
Age (years)	38.5	43.2
Cough	76	32
Night sweats	62	14
Hemoptysis	10	24
Fever	66	42
Weight loss	52	9

HRCT chest findings included cavitation, lymph adenoapthy, upper lobe consolidation, lobular consolidation, centrilobular nodules, tree in bud nodules, ground glass opacification, pleural effusion, interlobular septal thickening, predominance of S1, S2, S6 segments. (Table 2) (Fig 1-4)

Table 2: *HRCT Findings*

Variables	Number of patients (T=138)
Centrilobular nodules	80
Tree in bud configuration	92
Lobular consolidation	58
Lobar consolidation	52
Main lesion in S1, S2 or S6.	60
Ground glassing	66
Cavitation	60
Bronchiectasis	65
Pleural effusion	7
Mediastinal LAP	82
Reticulation	8

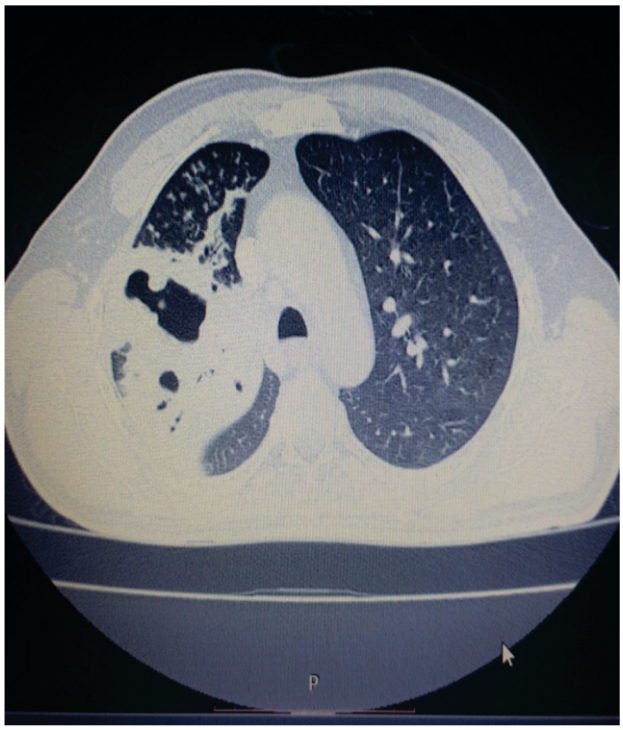

Fig 1: *Cavitation, Lobular Consolidation and Tree in Bud Nodularity.*

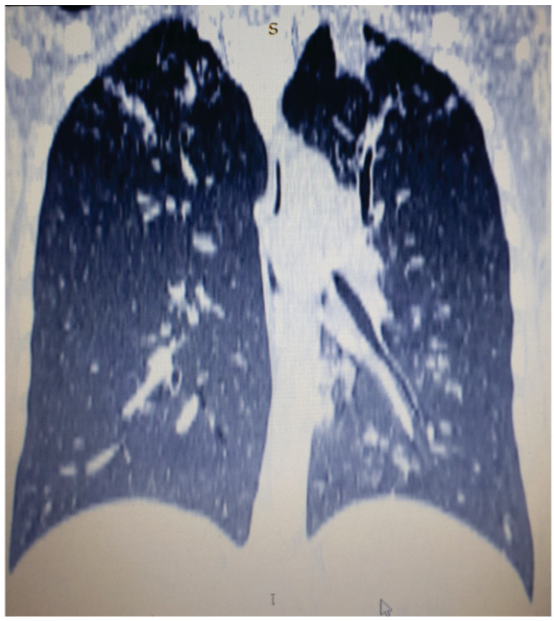

Fig 2: *S1, S2, S6 Predominant Pattern*

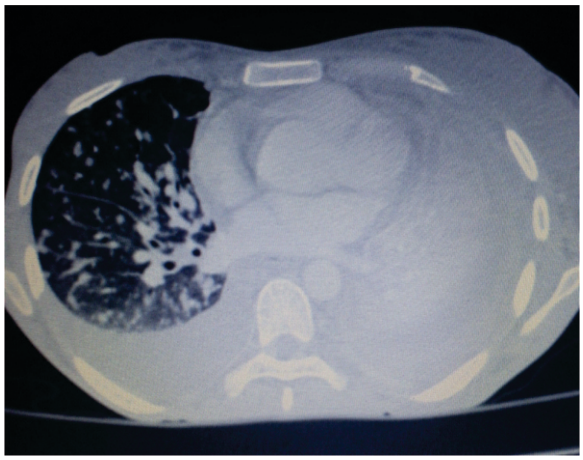

Fig 3: *S1, S2, S6 Predominant Pattern*

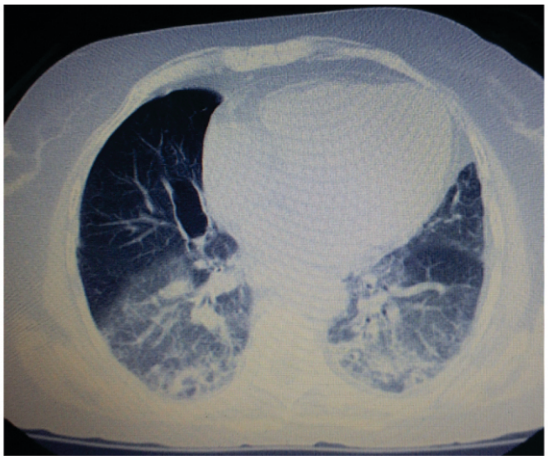

Fig 4: *Bronchiectasis, Reticulation and Ground Glassing*

Positions were formulated according to most observed findings in the imaging. (Table 3)

Table 1: HRCT Positions for Predicting PTB

Position	HRCT Criteria	Findings
1	Highly suspected	Presence of at least 3 of the following: main lesion in S1,S2,S6. tree in bud configuration. centrilobular nodules. lobular consolidation. cavitation. pleural effusion.
2	Probable	Presence of at least 2 of the following: main lesion in S1,S2,S6. tree in bud configuration. centrilobular nodules. lobular consolidation. cavitation. pleural effusion.
3	Non specific	No characteristic findings like ground glassing, honey combing, fibrosis, architectural distortion, emphysema.
4	Other disease	Some findings indicating other specific diseases.

PPV, NPV, Sensitivity and Specificity were calculated for each respective position. (Table 4)

Table 4: Sensitivity, Specificity, NPV,PPV for Each Position on HRCT

	Highly suspected	Probable	Non specific
Sensitivity	100%	87.9%	58.6%
Specificity	40.7%	91.4%	100%
Positive predictive value	5.56	28.22	-
Negative predictive value	0	0.23	0.48

DISCUSSION

PTB can be diagnosed using imaging and lab investigations.

Imaging includes chest x-rays and HRCT or CT chest. Chest X-ray is useful but is not specific for diagnosing pulmonary TB, and can be normal even when the disease is present9. Therefore, it needs to be followed by sputum testing10. PTB can be divided into primary and post primary TB. Primary TB findings include air space consolidation mainly at the bases, lymph adenoapthy (LAP) and pleural effusion. Chest X-ray findings in post-primary TB, include, cavitation, fibrosis and consolidations in apical or superior segment of lower lobes.[10]

HRCT chest is a sensitive investigation with PPV (96%) in differentiating active form inactive PTB[11]. It can detect tree in bud and centrilobular nodularity, tiny cavitations, consolidations and lymph nodal status. CT Chest may be useful in identifying active tuberculosis, however, it is not a standard investigation.[12]

Amongst the lab investigations, the gold standard for diagnosis of PTB is sputum gene Xpert.[13] It's an automated and cartridge based nucleic acid amplification test (NAA). It can not only detect the presence of MTB in sputum but also detect the resistance to rifampicin. It has been included for rapid molecular TB diagnosis in policy making and global implementation by WHO. However, its use is limited as it is not readily available in resource –limited hospitals.

Sensitivity and Specificity of Gene XPERT was 97.83% and 92.59%. However PPV, NPV and Diagnostic accuracy of Gene XPERT test was 96.77%, 94.94% and 96.23% respectively.[14]

Next lab investigation is conventional light microscopy of Ziehl-Neelsen-stained[15] (ZN) smears prepared directly from sputum specimens. ZN microscopy is highly specific, but its sensitivity is quite variable and hence, arguable. (20%-80%).[16]

Direct sputum smear microscopy is the also a widely used method for diagnosing pulmonary TB[17]. However, it is costly and inconvenient for patients, who must make multiple visits to health facilities and submit multiple sputum specimens over several days. The sensitivity is high and for two consecutive sputum specimens has been shown to be 95%-98%.[18]

Clinicians also obtain culture confirmation of TB whenever possible. However, it requires 4-8 weeks for diagnosis, which may delay the initial treatment.[19] This technique, although specific, has low and variable sensitivity and cannot identify drug-resistant strains.

Among the molecular methods of diagnosis the

nucleic acid amplification test has greater positive predictive value (PPV) (>95%) than smear micropsy.[20]

Fiberoptic bronchoscopy for the rapid diagnosis of smear-negative pulmonary tuberculosis is another tool but it is an aggressive, invasive and expensive investigation.[23] Line probe assay is another molecular method which is highly sensitive (>95%), but a complicated procedure and not available readily.[24]

Usually the algorithm followed in case of smear-positive patients is a chest xray and sputum culture.[21] In case of smear negative PTB, the gene Xpert has high sensitivity. It's very important to identify PTB early to prevent the spread of an epidemic. The rate of detection is already low due to non availability of state of the art investigations, multidrug resistant TB (MDRTB) and high prevalence of HIV/AIDS.

It was found that age and gender were not significantly associated with risk of PTB, though younger population is more prone to develop PTB in developing countries.[22] Among the clinical features, chronic cough, fever and night sweating was most common presenting complaint. This was followed by weight loss and hemoptysis.

A combination of HRCT findings of great concern were found. 60 patients had consolidation mainly in the apices S1, S2 or superior segments of lower lobes S6. Sensitivity was 100% and specificity was 70.8 % . Cavitation, though not specific to PTB, was found with 78% sensitivity and 90.7% specificity. Tree in bud nodularity is again not specific to PTB, is found in diseases with bronchiolar mucoid impaction namely ABPA, aspiration, infective bronchiolitis. Sensitivity was 100 % and specificity was 62%. Centrilobular nodules can be found in hypersensitivity pneumonitis, respiratory bronchiolitis, histiocytosis, interstiitial lung disease, connective tissue diseases and pulmonary infections along with PTB. The sensitivity and specificity of centrilobular nodules was found to be 87% and 87.4% respectively in our study. Although these findings are not discreetly associated with PTB, in combination they provide high sensitivity for anticipation of PTB.

CONCLUSION

The main purpose of this research was to establish the accuracy of HRCT in predicting risk of PTB and to formulate a predictability criteria for HRCT diagnosis of PTB so that it would help in selecting the patients for further invasive or advanced investigations. Significant similarity in HRCT findings was observed in patients with gene xpert positive results. Hence, our study concludes that HRCT is highly efficacious in predicting the presence of PTB in sputum smear negative patients. Thus, in cases of smear-negative PTB, the patients with compatible clinical and radiological features should be considered for tuberculosis treatment.

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RESULTS OF ACL RECONSTRUCTION UNDER IMAGE INTENSIFIER GUIDANCE

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Abstract

Background: Anterior cruciate ligament reconstruction is a technically demanding procedure and usually complications occur during surgery which results in failure of the procedure. Open and arthroscopic reconstructions are common techniques for ACL reconstruction. In this study CARM is used for reconstruction of ACL using BPTB graft.

Objective: To assess the functional outcome of ACL reconstruction, using BPTB graft Methodology: A total 35 cases were enrolled consecutively from the A/E and OPD, Lahoregeneral hospital, Lahore from 1-3 2018 to 28-2-2019 with complete ACL tear.Patients were evaluated by clinical examination and confirmed by MRI anddiagnostic arthroscopy. C-ARM was used for tunnel placement in the tibia and femur. BPTB graft was used in all patients who underwent ACL reconstruction. All patients were operated under tourniquet control. Weightbearing started on same day. Functional outcome was assessed in terms of stability, return of full motion, postoperative knee stiffness and comparing Lysholm score before and after reconstruction of ACL.Data was analyzed by SPSS 20. Functional outcome was presented as frequency and percentage for stability, full range of motion. Lysholm knee score was presented as mean and SD. Paired t test was used to assess improvement in lysholm knee score before and after reconstruction with $p < .05$ as statistical significance.

Results: Thirty five having ACL tear with 21(60%) patients had twisting injury during sports anf 14(40%) patients with Road traffic accident. 32(91.42%) patients did extremely well, with negative immediate postoperatively and weight bearing on average of 6-8 hrs. The mean satisfaction rate after 3 months was 7.1+- 0.6. The mean satisfaction rate after 6 months was 9.1+- 0.1. Before treatment, the stability grade-3 was observed in 22 (62.9%) and grade-2 was observed in 13 (37.1%) patients. After the treatment , Lachman was negative in 27 (77.1%) patients and grade-1 positive in 8 (22.9%) patients. Full range of movement was achieved in all, 35 (100%) patients at 12 weeks. The mean Lysholm knee score before surgery was 66.1 +- 5.6 and after surgery was 92.3 +- 4.3. The results show that there was remarkable improvement in Lysholm knee score after surgery with P-value < 0.001.

Conclusion: Using C-ARM improves accuracy and precision in placement of tibial and Interior femoral tunnels during reconstruction of torn ACL and reduces the incidence of common complications that results in failure of the surgery. This procedure is associated with minimal trauma to the patient and early mobilization with timely return to work so it should be first choice procedure to both the surgeon and the patient for ACL reconstruction in open and arthroscopic technique.

Keywords: ACL, Lysholm Knee Score, Image Intensifier

ACL is the main stabilizer of the knee joint.[1] ACL is also a commonly injured structure during Sports and other activities like jumping.[2,3,8] Tear of ACL causes instability symptoms and results in high morbidity.[2] Patients with ACL injury are unable to continue sports and other jobs which require vigorous activities like police, rangers and army personnel.[2] Majewski Metal in their study regarded sports sports to be the major cause of ACL injury.[26] Young people are more affected than elders.[4] Patients with ACL tear are unable to continue their previous activity and hence results in early retirement from their jobs.[1] The risk of injuries to the meniscus increases with ACL tear.[5] The risk of

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osteoarthritis also increases in long term cases, (Dekker Retal).[8] To overcome the problem associated with ACL tear , it should be reconstructed, in order to get the patient back to their previous activity level and work.[9] ACL reconstruction is necessary to make the knee stable and functional again so that the patient does not live with the fear of instability of his knee anymore.[10,11] If the ACl deficient knee is left untreated the patient will have symptoms of giving way, difficulty in walking on uneven surface, running and jumping which will disturb his life style.[11] For restoration and stability and function of the knee and to prevent long term complications. ACL should be reconstructed timely.[5]

Surgical reconstruction over several decades is done for ACL tear.[10,13] Various techniques have been evolved so far.[10] From repair to reconstruction and from open to arthroscopic reconstruction but all methods have certain complications which result in failure after ACL reconstruction.[12,22] To get better functional outcome of the reconstruction of ACL, graft placement in its anatomic position is mandatory.[3] Among the common reasons for failure after surgery is placement of the graft in non-anatomic position which results in worst outcome of the procedure.[24,28] It should also be kept in mind that the common technique used for ACL reconstruction is a single bundle and you can get on 60 to 70 % of the knee function.[34] Various grafts have been used among them BPTB graft and quadruple hamstring graft are common used grafts. Most surgeons like to use BPTB graft because of its mechanical strength and biological advantage over other graft choices.[17,18]

ACL reconstruction is still in the evolution phase and the reason being to overcome the complication and to improve outcome of the surgery.[19,20] Most common complicatin which occur during surgery that result in failure of the procedure in wrong tunnels placement other than its anatomic place.[12] This complication occurs both in open as well as in the arthroscopic ACL reconstruction. Few surgeions in the past like Goble, Helbrecht and Levy, Bernard and Hertel have used intra operative fluoroscopy for tunnel placementin the femur and tibia and defined landmark for the proper tunnel placement[10,11]. Trentacosta et al in 2014 studied in detail the use of C-ARM in transtibial ACL reconstruction and defined a 6-sector map for emoral tunnels placement with varying degrees of knee flexion[35]. Their results were very promising and patients showed better outcome with no cortical beaches and screw divergence. In this we will evaluate the functional outcome of the procedure in patients who will undergo ACL reconstruction with tunnel placement done under C-AR guidance. The rationale of this study is to produce the magnitude of the outcome as there is hypothetical knowledge or statements in the published literature. These hypothetical statements are based on the clinical or surgical experiences. Moreover no study was carried out on local level and international literature is not sufficient to reach a conclusion. Hence, the need of this study rises and we planned to execute this study. The result of this study will help us to make decision regarding the selection of appropriate surgical procedure for the above said cases.

METHODOLOGY

A clinical trial was done on a total 35 cases fulfilling selection criteria with anterior cruciate ligament tear after clinical examination and positive MRI finding of ACL tear were selected through a non-probability consecutive sampling from the A/E and OPD, Lahore general hospital, Lahore from 1-3 2018 to 28-2-2019 with complete ACL tear. Patients were evaluated by clinical examination and confirmed by MRI and diagnostic arthroscopy. Spinal anesthesia was given to most of the patients. Once under anesthesia the operative and non-operative legs were assessed again for range of motion, Lachman, Pivot Shift, Lateral and medial collateral ligament injuries.

C-ARM was used for tunnel placement in the tibia and femur. BPTB graft was used in all patients who underwent ACL reconstruction. All patients were operated under tourniquet control. Weight

bearing started on same day. Functional outcome was assessed in terms of stability, return of full motion, postoperative knee stiffness and comparing Lysholm score before and after reconstruction of ACL. Data was analyzed using SPSS version 20 Quantitative variables like age, time return to work was presented as mean of standard deviation. Qualitative variables like gender, stability return of full motion , postoperative knee stiffness and Lysholm knee scoring scale was presented in form frequency and percentage. Paired t-test was applied to determine the difference in LKSS before and after surgery. P-value <0.05 was considered as significant.

RESULTS

In this study, thirty five patients fulfilling selection criteria with ACL injury were enrolled from the outpatient Department of Orthopedics, Lahore General Hospital. Mean age group of patients was 26.7 +5.8. ACL tear with 21 (60%) patients with twisting injury during sports and 14 (40%) patients presented with road traffic accident. Before treatment the stability (LACHMAN TEST) grade-3 was observed in 22 (62.9%) patients and grade-2 was observed in 13 (37.1%) patients. After the treatment, Lachman was negative in 27 (77.1%) patients and grade-1 positive in 8 (22.9%) patients. Lysholm score was also calculated before and after surgery. The mean Lysholm knee score before surgery was 66.1 + 5.6. (Table 1). The mean Lysholm knee score 6 months after surgery was 92.3 + 4.3. Paired T- test was used to determine the mean difference before and after surgery. The results showed that there was significant improvement in Lysholm score after surgery with P-value <0.001.(Table 3). There was only 1 patient (2.9%) who had reactive arthritis (resolved with antibiotics) whereas in 34 (97.1%) patients no infection was observed, Surgical site infection rate was also zero.Full range of movement was achieved in all 35(100%) of the patients after 6 months. No patient presented with knee stiffness and full flexion and extension was noted in all 35 (100%) of the patients.

Table 1: Demographic and Clinical Profile of Subjects

Variables	Frequency	Percentage
Age mean=26.7 SD ± 5.8.		
< 40	19	54.3
> 40	16	44.6
Knee Involvement		
Right	23	65.7
Left	12	34.3
ACL Tear		
Isolated ACL injury	21	60.0
Meniscal injury	14	40.0
Mode of injury		
Twisting injury during sports	21	60.0
Road traffic accident	14	40.0
Stability of knee (Lachman test) Before treatment		
Grade 2	13	37.1
Grade 3	22	62.9
Stability of knee (Lachman test) After treatment		
Negative	27	77.1
Grade 1 postive	8	22.9
Infection		
Yes	1	2.9
No	34	97.1

Table 2: Stability Score before and After Treatment

Treatment	Stability score				Total
	Score 0	Score 1	Score 2	Score 3	
Before	0 (0.0%)	0 (0.0%)	13(37.1%)	22 (62.9%)	35(100%)
After	27 (77.1)	8(22.9%)	0 (0.0%)	0 (0.0%)	35(100%)

Table 3: Lysholm Knee Score Before and After Treatment

Lysholm Knee Score	Mean	SD	P-value
Before Surgery	66.1	5.6	<0.001
After Surgery	92.3	4.3	

DISCUSSION

Anterior cruciate ligament injury is common ligamentous injury of the knee joint. Incidence of ACL injury has been increased due to active participation in sports and road traffic incidents these days. Anterior cruciate ligament injury causes symptoms of instability of the knee when patient walks on uneven surface and take participation in sporting activities.

The incidence of ACL tear is variable in different studies and less studies have been published which report the type and frequency of knee

injuries.[25] M. Majewski et al in their study over 10 year period reported ACL injury to be the most common injury of the knee joint and most common in males (68.1%) in age group 22-29.[25,26]

ACL deficient knees other than instability symptoms can lead to frequent meniscal tear and cartilage damage and results in early onset osteoarthritis. Kenneudy et al suggested that acute ACL tear should be reconstructed after his study on 50 patients which were treated for ACL tear. He managed 19 patients with ACL tear surgically and 31 patients conservatively without surgery. He did a long follow up of 7 years. The patients which he operated had good functional outcome as compared to the patients whom he managed conservatively without surgery. Therefore, he recommended that anterior cruciate ligament need to be reconstructed to make the knee stable again.

In our study, 35 patients completed the 6 months follow-up. The mean age group of patients was 26.7 + 5.6. 21(60%) patients were with twisting injury during sports and 14(40) patients presented with road traffic accident. The mean of Lysholm knee score 6 months after surgery was 92.3 + 4.3.

The incidence of meniscal tear with ACL injury varies. In one study by Mansori AE et al, their results show that the patient medial meniscus is the most common tear. In our study Isolated ACL injury was involved in 21 (60.0%) patients while medial meniscus Meniscal injury was involved in 14 (40.0%) patients.[23]

In another study Prasad Veergandham et al studied 36 patients with ACL tear.[30] In his study Right side ACL injury in 25 patients (69.44%) and left side ACL injury was in 11 (30.55%) patients.[30] RTA was the common mode of injury in his study and involved 19(52.77%) patients while sports related injuries were involved in 10 (27.77 %) while 7 patients had ACL tear due to domestic activities like slipping on the floor or fall from a ladder. 25 (69.44%) patients had isolated ACT injury and 11 patients had associated injuries. In our study, Right knee involved in 23 (65.7%) while Left knee was involved in 12 (34.3%). Isolated ACL was involved in 21 (60%) patients and Meniscal injury was involved in 14 (40%) patients. In our study patients having ACL tear with 21(60%) patients with twisting injury due to sports activity and 14 (40%) patients presented with road traffic accident.[30]

In our study by Syed Danish Ali et al functional outcome after ACL reconstruction using BPTB graft was assessed by Lysholm Knee Score using short term follow up of 6 months and their results showed that half of their patients achieved good results, while half had fair functional outcome. In our study pre-op and post-op Lysholm knee scoring were compared after ACL reconstruction using BPTB graft. The mean of Lysholm Knee Score before surgery was 66.1+ 5.6. The mean of Lysholm Knee Score 6 months after surgery was 92.3 + 4.3 showing excellent improvement in knee function before and after surgery.[33]

In our study patients satisfaction rate was also studied by using a Performa about knee function of the patients before and after surgery and results were assessed after surgery at 3 months and 6 months. The mean satisfaction rate after 3 months was 7.1 + 0.6. The mean of satisfaction rate after 6 months was 9.1 + 0.1. The data show that there was significant improvement in patient satisfaction rate after surgery.

In another study knee range of movements were assessed by Veerganham et al and there results showed that only 4 (11.11%) patients had restrictions in knee range of motion while most of the patients 26 (72.22%) had fully normal flexion and extension. In our study all 35 (100%) had full range of motion of the knee for 0 to 145 degree and no patient was reported to have any knee stiffness with normal knee flexion and extension.[30] We found out that post-operative rehabilitation has an important role in regaining full range of movement of the knee joint and avoiding knee stiffness which is common after knee surgery. Pre-operative counseling and explaining to the patient is the importance of rehabilitation program and its significant results in better functional outcome of the procedure. The role of the pre-op and post-op rehabilitation was studied by Biggs A et al and there result showed that when active rehabilitation program is used , all the patients achieve

normal knee extension and knee flexion.[1]

We also studied stability of the knee joint immediately after surgery with Lachman test and graded it as Grade-1 with 3-5mm translation. Grade-2 with 5-10mm translation and Grdae-3 more than 10mm translation and compared it with pre surgery grade. We found out Lachman test was negative in 27 (77.1%) patients and grade-1 positive in 8 (22.9%) patients. These 8 patient with grade 1 positive Lachman after surgery were the first cases we operated and the reason position of thtibial side interference screw fixation that had to be in 30 degree flexion, internal rotation and anterior draw of the proximal tibia. That was the learning curve of the procedure and we overcome that with time the procedure our results were improved with immediate negative Lachman after the ACL reconstruction in the remaining 27 patients.[13]

Now coming to the method of ACL reconstruction, currently open and arthroscopic technique are commonly used for ACL reconstruction. Open technique are commonly used for ACL reconstruction. Failure rates with ACL reconstruction has been high and in review of many articles we have found out that tunnel placement, graft-tunnel mismatch and screw placement are the main reasons for the failure regardless of whatever method is used. Among these complications, Gobble et al in 1988 use C-ARM for transtibial ACL reconstruction after his work he pointed out certain landmarks for tibial and femoral tunnel placement. After the work of Gobble, Halcrecht and Levy described the role of C-ARM in ACL reconstruction to decrease the complications occurring during surgery which results in failure of the procedure. Finally in 2014 Natasha Trentacosta et al studied briefly on the use of C-ARM during ACL reconstruction and designed a 6-sector for femoral tunnel placement. They analyzed 112 reconstructed over the period of 3 years and there results showed that there was no cortical breach, no graft-tunnel mismatch when thay used C-ARM during the procedure.[35]

In this study we have also used C-ARM for tibial and femoral tunnel placement using the 6-sector map with varing flexion angle at the knee and analyzed the functional outcome of the procedure. Our results were incredible. We used BPTP graft which is considered to be gold standard graft for ACL reconstruction. We searched is not as easy procedure. A surgeon who is performing ACL reconstruction should have full understanding of the anatomy and function of the ACL and should have a sound knowledge of the common complications which occur during ACL reconstruction which results in the failure of the procedure. A surgeon should know the type of graft and length he is taking and then exact position of the tunnels in tibia and femur. Then graft passage through the tunnels and final the position and angle of the joint in which the graft is fixed with interference screws. Although this is a limited study with a short follow-up but I think it will help in future fellows to come up with new ideas and work on this topic and help us in improving this technique. We have made every attempt to make this procedure simplified for the new surgeons which will ultimately help the patients and will result in better outcome of the procedure.

CONCLUSION

Using C-ARM improves accuracy and precision in placement of tibial and femoral tunnels during reconstruction of torn ACL and reduces the incidence of common complications that results in failure of the surgery. This procedure is associated with minimal trauma to the patient and early mobilization with timely return to work so it should be first choice procedure to both the surgeon and the patient for ACL reconstruction in open and arthroscopic technique.

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EPIDEMIOLOGY AND HISTOPATHOLOGICAL SPECTRUM OF LESIONS IN HYSTERECTOMY SPECIMENS IN GULAB DEVI HOSPITAL, LAHORE

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Abstract

Background: Hysterectomy is the major gynaecological procedure performed in females for various uterine pathologies including both benign and malignant lesions.

Objective: Objective of this study is to assess the frequency of different uterine pathologies based on histopathology including endometrial, myometrialand cervical neoplastic and non neoplastic lesions.

Methods: This was adescriptive case series conducted in histopathology and gynaecology department of Gulab Devi Teaching Hospital. 125 Hysterectomy specimensof females of 41 to 55 years with or without sapingo oophorectomy were included in the study for a duration of 18months from January 2018 to May 2019. Indications of hysterectomy, type of hysterectomy; abdominal or vaginal were noted on performa. The variables noted on histopathology were cervicitis, endocervical polyp, cervical carcinoma, endometrial polyps, endometritis, phases ofendometrium, adenomyosis, leiomyoma and endometrial carcinoma . Data was entered and analyzed on SPSS.

Results: Of total 125 hysterectomies, 105 cases had undergone abdominal and 20 cases had under went vaginal hysterectomy. Maximum patients 104 females (83.2%)were in the age group of 41-49 years. The most common indication for hysterectomy was dysfunctional uterine bleeding 72cases (57.6%).Chronic cervicitis81 cases(64.8%) was the most common cervical pathology and carcinoma cervix 1case (0.8%). 25(20%) cases revealed disordered proliferative endometrium and endometrial carcinoma in 1(0.8%)cases. There were 66cases (52.5%) of leiomyomas followed byadenomyosis36(28.8%)cases. The maximum cases of leiomyoma and adenomyosis were observed in age group of 41-50 years.

Conclusion: This study concludes that histopathological evaluation of hysterectomy specimens is an important diagnostic tool to detect malignancy guiding patient management. This study has shown that leiomyoma is the most common benign lesion in uterus and squamous cell carcinoma and endometrial carcinoma are the malignant lesions seen.

Key words: hysterectomy, histopathological lesions

Hysterectomy is the most common major gynaecological surgical procedure done in females both for benign and malignant lesions. Most common indications of hysterectomy are abnormal uterine bleeding, fibroid, adnexal mass, and uterovaginal prolapse. Two types of hysterectomy done are abdominal hysterectomy for fibroids, adnexal mass and vaginal hysterectomy for utero-vaginal prolapse. Each specimen is sent for histo-pathological assessment on which gross and microscopic features are studied and compared with the indications.

Multiple benign or malignant conditions can be diagnosed on histopathology [(1)]. The histopatholo-

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gical diagnosis of hysterectomy specimens includes chronic cervicitis, endometritis, endometrial hyperplasia, atrophic endometrium, leiomyomas, adenomyosis. These histopathological diagnosis in a study revealed that endometrial hyperplasia was the commonest finding.[2] Most of the diagnosis were of benign conditions such as hormonal imbalance, endometritis, adenomyosis. Another study found uterine fibroid and adenomyosis were most common benign conditions diagnosed by histopathology.[3] Indications of hysterectomy were dysfunctional uterine bleeding, fibroid, postmenupausal bleeding or uterine prolapsed. The histopathological spectrum was fibroid in 36.5%, adenomyosis 28%, endometrial hyperplasia 12% and malignancies in 5% of cases.[4] The rationale of this study is to find out different histopathological patterns in hysterectomy cases presenting in inpatient department of Gulab Devi Hospital and to analyze the disease burden in this setting.

OBJECTIVE

1) Objective of this study is to study the different diagnosis based on histopathology and formulate further treatment.
2) To diagnose the endometrial or pelvic malignancy and counsel the patient for early management.

Study Design

Retrospective, observational, cross sectional

Study Duration

Duration of study is from January 2018 to May 2019

METHODOLOGY

This will be a retrospective study conducted in histopathology and gynaecology department of Gulab Devi Teaching Hospital. Data will be collected from records of histopathology and gynae departments. Hysterectomy specimens of females of 41 to 55 years with or without sapingo oophorectomy will be included in the study. Indications of hysterectomy, type of hysterectomy abdominal or vaginal will be noted on performa. The variables that will be noted on histopathology are cervicitis, endocervical polyp, cervical carcinoma, endometrial hyperplasia, endometrial polyps, endometritis, atrophic endometrium, adenomyosis, leiomyoma, endometrial carcinoma. The frequency and percentage will be found by descriptive analysis. Mean age of the patient will be calculated. Analysis of histopathology results will be done. .

Inclusion Criteria**:** Hysterectomy specimens received in histopathology lab in females of 41-55yr

Exclusion Criteria: Hysterectomy specimens after cesarean hysterectomy

Data Collection: From histopathology and gynaecology depart-ment of Gulab Devi teaching hospital

Sample Size: 125 cases.

Statistical Analysis: All data will be entered and analyzed on SPSS.

RESULTS

Hysterectomy is the major gynaecological surgery done worldwide for symptomatic cure of patients. We conducted this study in Gynaecology and Histopathology department of Al Aleem Medical college / Gulab Devi teaching hospital, Lahore. It is a retrospective study. A total of 125 patients were included in this study for a duration of 18months from January 2018 to May 2019. This study was conducted to analyse the histopathological spectrum of lesions in hysterectomy specimens and to assess their frequency in our institution and to compare the findings with other studies. In this study out of 125 cases, 105 cases had undergone TAH, 20 cases had undergone vaginal hysterectomy.

In the present study the maximum number of patients who had undergone hysterectomy were in the age group of 41-49 years . (Table 1). There were 104 females (83.2%) in the age group between 41-

Table 1: Age Distribution of Patients with Hysterectomy

Age group	No of cases (Frequency)	Percentage
41- 49yrs	104	83.2%
>50 yrs	21	16.8%

Table 2: Indications of Hysterectomy

Indication of hysterectomy	No of cases (Frequency)	Percentage
Dysfunctional uterine bleeding	72	57.6%
Fibroid	40	32%
Endocervical and endometrial polyp	11	8.8%
Uterovaginal prolapse	2	1.6%

Table 3: Histopathological Diagnosis of Lesions of Cervix

Histopathological diagnosis	No of cases (Frequency)	Percentage
Chronic cervicitis	81	64.8%
Squamous metaplasia	39	31.2
Endocervical polyp	4	3.2%
Squamous cell carcinoma	1	0.8%

Table 4: Histopathological Diagnosis of Endometrial Lesions

Histopathological diagnosis	No of cases (Frequency)	Percentage
Proliferative phase endometrium	75	60%
Secretory phase endometrium	8	6.4%
Atrophic endometrium	7	5.6%
Disordered proliferative endometrium	25	20%
Chronic Endometritis	3	2.4%
Endometrial polyp	6	4.8%
Endometrial carcinoma	1	0.8%

Table 5: Histopathological Diagnosis of Myometrial Lesions

Histopathological diagnosis	No of cases	Percentage
Leiomyoma	66	52.5%
Adenomyosis	36	28.8%
Normal histology	23	18.4%

49 years and 21 females (16.8%) above 50 years who underwent hysterectomy. The present study revealed that the most common indication for hysterectomy was dysfunctional uterine bleeding (Table 2). 72cases (57.6%) of dysfunctional uterine bleeding followed by fibroid 40 cases (32%), endocervical and endometrial polyp 11 cases (8.8%), and uterovaginal prolapse 2 cases (1.6). (Table 2)

Cervical pathologies include Chronic cervicitis with or without squamous metaplasia. Of total 125 cases, 81 cases(64.8%) were of chronic cervicitis followed by 39 cases (31.2%)of squamous metaplasia. Endocervical polyp was seen in 4cases (3.2%) followed by carcinoma cervix in 1case (0.8%). (Table 3).

Endometrium pathologies include proliferative phase endometrium 75 (60%) cases followed by 8 (6.4%) cases in secretory phase, 7 (5.6%) cases of atrophic endometrium and 25(20%) cases revealed disordered proliferative endometrium. Endometrial polyps were observed in 6(4.8%) cases. Chronic endometritis was seen in 3(2.4%) cases and endometrial carcinoma in 1(0.8%)cases. (Table 4)

Myometrium pathologies include 23 cases (18.4%) with normal myometrial histology. There were 66(52.5%)cases of leiomyomas followed by adenomyosis 36(28.8%) cases. The maximum cases of leiomyoma was observed in age group of 41-50 years.

Adenomyosis was also found most frequently in 41-50 years of age. (Table 5)

DISCUSSION

Hysterectomy is the commonest gynaecological surgical procedure in females. It is the second most common surgical procedure in USA. 5 per 1000 females underwent hysterectomy in USA each year making it the second most common procedure done in USA5. It is a reliable, curative and effective treatment strategy for various uterine pathologies including both benign and malignant lesions.

Hysterectomy can be done via abdominal and vaginal route. In this study abdominal hysterectomy is done in 105cases (84%) and vaginal hysterectomy in 20 cases (16%). Patil et al have reported TAH in 38.0% cases[6]. GR et al have reported TAH in 67.19% cases[7]. The variation in the percentage of type of hysterectomy may be due to patient and operating surgeon convenience. It is seen in this study and comparable other studies that abdominal approach was the prefered methodology of surgery. In this study it was seen that majority of hysterectomies were done in age group 0f 41-49 years i-e 104 cases (83.2%) as compared to 21 cases (61.8%) in age > 50 years. A study done by Gupta et al[7] revealed that maximum number of hysterectomies done were in the age group 41-49 years. This is comparable with the study done at Gulab Devi teaching hospital. In this study most common indication of hysterectomy was dysfunctional uterine bleeding 72 cases (57.6%) followed by fibroid 40 cases (32%) and

uterovaginal prolapse in 2 cases (1.8%). Menorrhagia was the most common indication in similar studies by Rather et al,[8] (35.43%) and Saleh et al,[9] (39%) whereas uterovaginal prolapse was the commonest indication in a study by Jha et al.[10]

In our study, the most common histopathological diagnosis in cervical lesions is chronic cervicitis 81 cases (64.8%) and squamous cell carcinoma comprising 1 case (0.8%). These results are comparable with the study done by Jain A et al[11] with chronic cervicitis comprising 70cases(35%) and squamous cell carcinoma 6cases (3%). Among endometrial pathologies the most common histopathological diagnosis was proliferative endometrium 75 cases (60%) followed by disordered proliferative endometrium 25 cases (20%), endometrial polyp 6 cases (4.8%), chronic endometritis 3 cases (2.4%) and 1 case (0.8%) of endometrial carcinoma was reported. These results are comparable with study done by Singh P et al[12] showing proliferative endometrium (38.36%), disordered proliferative endometrium (6.19%), endometrial polyp (4.70%), chronic endometritis (1.48%), endometrial carcinoma (0.50%).

Among myometrial pathologies leiomyoma was the most common diagnosis followed by adenomyosis. Study done by Singh et al[12] also showed the comparable results with leiomyoma (20.53%) most common histopathological diagnosis followed by adenomyosis (14.32%).

CONCLUSION

Histopathological evaluation of hysterectomy specimens is an important diagnostic tool to differentiate between benign and malignant lesions of uterus and can detect malignancy guiding patient management. This study has shown that leiomyoma is the most common benign lesion in uterus and squamous cell carcinoma and endometrial carcinoma are the malignant lesions seen on histopathological analysis of hysterectomy specimens.

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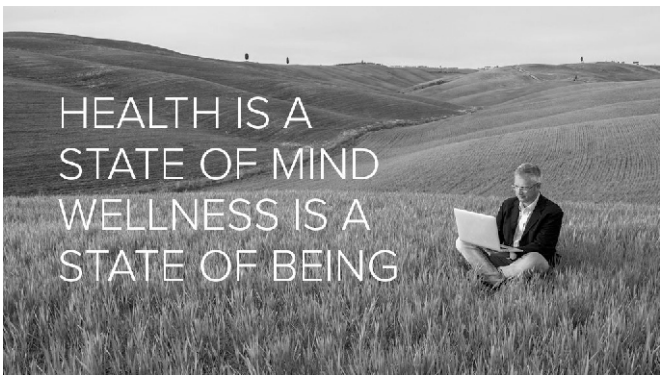

COMPARISON BETWEEN PRE-OPERATIVE KETAMINE AND MAGNESIUM SULPHATE GARGLES FOR PREVENTION OF POST OPERATIVE SORE THROAT IN AMBULATORY SURGERY

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Abstract

Background: Post operative sore throat is a common and very distressing problem encountered after general anaesthesia with endotracheal intubation, reducing patient satisfaction particularly after ambulatory surgery. We carried out this study to compare the efficacy of maganesium gargles with that of ketamine done pre operatively for the reduction in the incidence and severity of post operative sore throat.

Methodology: This randomized controlled trial was carried out from Feb 2018 to July 2018. 100 patients were recruited for this study having age between 20 to 65 years, both male and female gender, patients belonging to ASA class I and II, having weight upto 80 kgs, scheduled for day care surgeries under general anaesthesia with endotracheal intubation and having Mallampatti score of 1 or 2. Patients were divided in two groups, A and B (50 patients in each group). Patients in group A gargled with magnesium sulphate, 20mg/kg in 30 ml of 5% dextrose water while patients in group B gargled with ketamine, 0.5mg/kg in 30 ml of 5% dextrose water, for 30 seconds 15 minutes before the induction of anaesthesia. Presence or absence of POST and its severity was noted in the immediate post operative period, 2hrs, 4hrs, 6 hrs and 12 hrs after the surgery was over. The severity of POST was graded according to the four point scale.

Results: The two groups were comparable in terms of age, gender distribution and weight, duration of surgery, ASA class and Malampatti score. The incidence of POST in both groups was also comparable at time 0 ($p = 0.839$) and 2hrs ($p = 0.309$). However, the incidence was significantly lower in group A than in group B at 6 hr ($p=0.024$), 12 hr (0.012) and 24 hrs ($p=0.029$) post surgery. The severity of POST was significantly lower in group A as compared to group B at 12 hr ($p=0.041$) and 24 hrs ($p=0.049$) post surgery.

Conclusion: Magnesium sulphate gargles are effective in reducing the incidence and severity of post operative sore throat as compared to ketamine gargles.

Keywords: Ketamine, Nagnesium sulphate, Post operative sore throat, Ambulatory surgery.

Postoperative sore throat (POST) is a minor yet one of the commonest and distressing experiences encountered by the patients undergoing surgeries under general anaesthesia with endotracheal intubation.[1,2] The problem becomes even more significant when patients have undergone some daycare surgery as it adds to their dissatisfaction and increases hospital stay.[3,4] Studies have shown that the incidence of POST is around 14.4-90%, thus highlighting the magnitude of the problem.[5]

Many options for the prevention of POST have been offered but none has proved to be exceptionally successful. Drugs like steroids, opioids, non steroidal anti inflammatory drugs have been used preemptively for prevention as well as for the treatment of POST with variable success.[1]

Both Ketamine and magnesium sulphate are antagonists of NMDA receptors[2,3] thus having

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analgesic effect. As NMDA receptors are also present in the peripheral nerves,[6] these drugs can be useful for preventing POST when used locally as gargles.

In our study, we have compared the efficacy of these drugs when used locally as gargles for POST. The results will help to reduce the incidence of POST in day care patients, thus enhancing their comfort and satisfaction in post operative period, expediting their discharge while using easily available drugs used locally, with minimal side effects.

METHODOLOGY

This randomized controlled trial was carried out in the operating rooms of Mayo Hospital Lahore, from Feb 2018 to July 2018. 100 patients undergoing surgical procedures under general anaesthesia were recruited for this study calculated with 80% power of test, level of significance 0.05, 95% confidence level using sample size calculator, assuming the incidence of POST 60%. Clearance regarding ethical issues of this study was taken from the ethical committee, Mayo hospital, Lahore. Inclusion criteria were age between 20 to 65 years, both male and female gender, patients belonging to ASA class I and II, having weight upto 80 kgs, scheduled for day care surgeries under general anaesthesia with endotracheal intubation and having Mallampatti score of 1 or 2. Patients having hypersensitivity to ketamine or magnesium sulphate (based on history), history of sore throat before surgery, patients with hepatic, renal or cardiovascular diseases, hypertensive patients, diabetic patients, smokers, pregnant and lactating women were excluded from the study. Patients whose surgical duration lasted more than 2 hrs were also excluded from the study.

Patients fulfilling inclusion criteria were taken to operating room after informed consent. They were divided in two groups, A and B. Patients in group A gargled with magnesium sulphate, 20mg/kg in 30 ml of 5% dextrose water while patients in group B gargled with ketamine, 0.5mg/kg in 30 ml of 5% dextrose water, for 30 seconds 15 minutes before the induction of anaesthesia. Standard monitors such as pulse oximeter, Electrocardiogram (ECG) and Non-invasive blood pressure monitor (NIBP) were applied. Preoxygenation for 5 mins with 100% oxygen was done. Induction of anaesthesia was carried with injection propofol till the loss of verbal command (1.5 to 2 mg/kg) and injection atracurium, 0.5 mg/kg. Endotracheal intubation was done after 3 minutes of atracurium administration. Cuff of endotracheal tube (ETT) was filled with minimum amount of air till the audible air leak vanishes. Patients in whom more than one attempt was made for intubation were excluded from the study. Anaesthesia was maintained with isoflurane in 50% oxygen and 50 % nitrous oxide. Injection nalbuphine 0.1mg/kg intravenously and injection Paracetamol 15mg/kg intravenously were used for analgesia in all the patients. All the haemodynamic parameters including SpO_2, ECG, NIBP and $EtCO_2$ were continually monitored. After the completion of surgery, neuromuscular blockage was reversed by giving injection neostigmine 2.5 mg and injection atropine 1mg, intravenously. Oral suctioning was done under direct vision using yankauer suction tip and patients were extubated after adequate spontaneous ventilation was established and patients were fully awake. Presence or absence of POST and its severity was noted in the immediate post operative period, 2hrs, 4hrs, 6 hrs and 12 hrs after the surgery was over. The severity of POST was graded according to the four point scale ranging from 0 to 3; 0 = no sore throat, 1 = mild sore throat (complains only upon inquiring), 2 = moderate sore throat (complains on his/her own but with no voice change) and 3 = severe sore throat accompanied by change in voice. All the observations and demographic details of the patients were noted on predesigned Proforma.

The data was analyzed using SPSS version 20. Mean was calculated for quantitative variables like age of the patients, weight of the patients and duration of surgery. Independent sample t-test was applied as a test of significance. For qualitative variable like gender, ASA class, Malampatti score

and incidence of POST frequency was calculated and Pearson's chi square test was used as a test of significance. Fisher's exact test was carried out to compare the severity of POST between two groups. P value of < 0.05 was taken as significant.

RESULTS

The two groups were comparable in terms of age, gender distribution and weight, duration of surgery, ASA class and Malampatti score (Table 1). The incidence of POST in both groups was also comparable at time 0 (p = 0.839) and 2hrs (p = 0.309). However, the incidence was significantly lower in group A than in group B at 6 hr (p=0.024), 12 hr (0.012) and 24 hrs (p=0.029) post surgery (Table 2). The severity of POST was significantly lower in group A as compared to group B at 12 hr (p=0.041) and 24 hrs (p=0.049) post surgery (Table 3).

Table 1: Comparison of Demographic Data of Two Groups A and B

PARAMETER	GROUP A		GROUP B		P-VALUE
AGE in years (mean)	**38.84± 12.42**		**41.00 ± 13.69**		**0.411**
GENDER	Male	Female	Male	Female	0.841
	25 (50%)	25 (50%)	24 (48%)	26 (52%)	
ASA CLASS	ASA-I	ASA-II	ASA-I	ASA-II	0.673
	34 (68%)	16 (32%)	32 (64%)	18 (36%)	
MALAMPATTI SCORE	I	II	I	II	0.688
	28(56%)	22 (44%)	26 (52%)	24 (48%)	
DURATION OF SURGERY IN MINS (mean)	67.90 ± 24.766		63.00 ± 24.826		0.326
WEIGHT OF PATIENTS in kgs. (mean)	59.80 ± 9.517		59.36 ± 10.034		0.822

Table 2: Comparison of Incidence of Post Between Group A And Group B

TIME (hrs)	INCIDENCE OF POST IN GROUP A	INCIDENCE OF POST IN GROUP B	P - VALUE
0 (immediate post op)	40%	42%	0.839
2	36%	46%	0.309
6	28%	50%	0.024
12	24%	48%	0.012
24	20%	40%	0.029

Table 3: Comparison Of Severity Of Post Between Group A And Group B

TIME (hrs)	SEVERITY SCORE OF POST	No. of Patients GROUP A	No. of Patients GROUP B	P VALUE
0 (immediate post op)	0	30	29	1.00
	1	20	21	
	2	00	00	
	3	00	00	
2	0	32	27	0.416
	1	18	22	
	2	00	01	
	3	00	00	
6	0	36	25	0.087
	1	13	21	
	2	01	03	
	3	00	01	
12	0	38	26	0.041
	1	10	21	
	2	02	03	
	3	00	00	
24	0	40	30	0.049
	1	10	19	
	2	00	01	
	3	00	00	

DISCUSSION

In the past decades anaesthesia practice has been revolutionized. The incidences of adverse events have reduced manifold. Despite this fact, a minor yet very much distressing complication of post operative sore throat continues to be a common complaint of the patients after endotracheal intubation.[7,8] Among various factors that lead to increase in the incidence of POST, use of endotracheal tube during general anaesthesia is one.[9,12] Higher incidence of POST and pain leads to increase in the consumption of analgesics in the post operative period which comes with its own set of adverse effects.[7]

In this study we compared the effect of preoperative gargles of magnesium sulphate with ketamine for reduction in the incidence of POST. The results of our study showed that gargles with magnesium sulphate are superior to that of ketamine in this regard. Also the severity of POST in the magnesium group was lower as compared to the ketamine group. Hence, as a result of our study,

magnesium sulphate has emerged as a better agent for the prevention of POST. Antagonism of NMDA receptors by magnesium appears to the underlying mechanism for this pre-emptive analgesic effect.[2,3,14] Although the mechanism of analgesic action of ketamine is also by blocking NMDA receptors,[2] results of our study indicate that the topical action of magnesium is better than that of ketamine.

The results of our study are comparable to that conducted by Teymourian et al.[2] Their study too established magnesium sulphate gargle superior to that of ketamine for the prevention of POST. However, in their study, the incidence and severity were significantly lower in magnesium group at 2hr post surgery and onwards whereas in our study the incidence was significantly lower in magnesium group at 6hr and onwards. Although in our study the severity of POST was less in magnesium group at 2 and 6 hrs post surgery, the difference was not significant; the difference was significantly lower in magnesium group as compared to ketamine group 12hrs post surgery and onwards. Studies comparing the efficacy of magnesium with ketamine for POST are also scarce. Canbay et al compared the effect of ketamine gargles with placebo on POST and concluded that ketamine gargles significantly attenuates the incidence and severity of POST.[6] Rudra et al also had similar results in their study on ketamine gargles for POST.[15] This indicated that patients may vary in their response to ketamine gargles, which could also be dose dependant. However, increasing the dose may invite unwanted side effects of ketamine. Results of study conducted by Ahuja et al showed that Ketamine nebulization compared with saline also reduces the incidence and severity of POST in early post operative period.[16] Magnesium sulphate nebulization compared with saline by Yadav et al showed magnesium significantly better in reducing the incidence of POST.[3] Safavi et al gave intravenous dexamethasone to the patients along with ketamine gargles and concluded that using intravenous dexamethasone along with ketamine gargles effectively reduces the incidence and severity of POST compared to either of these agents used alone.[17] Rajan et al conducted a randomized controlled trial comparing the efficacy of nebulized magnesium with nebulized ketamine for attenuation of POST and concluded that both of these drugs are effective as compared to placebo in this regard.[18] Various other studies have shown that drugs like inhaled budesonide, zinc lozenges and betamethasone gel lubrication of endotracheal tube also useful for reducing the severity and incidence of POST[12,19,20]. The dose of ketamine used in our study was 0.5mg/kg. Whether an increased dose makes it an effective agent for attenuation of POST and presence or absence of unwanted side effects at such dose needs to be studied.

CONCLUSION

Regarding the prevention and reduction in the severity of post operative sore throat, gargles with magnesium 15 mins prior to intubation are more effective than ketamine gargles.

However, further studies are needed regarding the increased dose of ketamine in gargles and any adverse effects related to it see if it effectively prevents and decrease the intensity of POST.

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ASSOCIATION OF CHRONIC HYPERTENSION WITH DEVELOPMENT OF GESTATIONAL DIABETES MELLITUS DURING SECOND TRIMESTER OF PREGNANCY

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Abstract

Background: Hypertension and gestational diabetes mellitus have various common pathogenic pathways and there is an underlying association between the two conditions. Insulin resistance is known to be involved in the pathogenesis of gestational diabetes mellitus and it has been found to be a contributing factor to chronic and gestational hypertension and gestational diabetes mellitus.

Objective: To determine that chronic hypertension in pregnancy is associated with development of gestational diabetes mellitus during second trimester of pregnancy.

Methodology: This case control study was conducted in the Department of Obstetrics & Gynaecology, Lady Aitchison Hospital, Lahore from July to December 2017. A total of 226 cases (113 in each group) were included by non-probability consecutive sampling. Females of age: 25 - 45 years of parity <5 presenting at Gestational age>24 weeks on LMP were included. Women with GDM (were taken as cases while women without GDM were taken as control. Informed consent and Demographic information was obtained. These women were divided in two groups. Then BP of females assessed and history of hypertension obtained. Data was entered and analysis through SPSS 22. Odds Ratio was calculated OR>1 was considered as risk and was taken as significant.

Results: During pregnancy, women with history of chronic hypertension at least for five years had a risk of GDM (Relative risk 1.90 [95% CI 0.95-3.81]), with significant p value of 0.06.

Conclusion: There is significant association between gestational diabetes mellitus and chronic hypertension.

Key words: Chronic Hypertension, Gestational Diabetes Mellitus

Chronic hypertension in pregnancy is defined as a blood pressure of at least 140 mm Hg systolic or 90 mm Hg diastolic pressure before pregnancy or, for women who first present for care during pregnancy, before 20 weeks of gestation. The prevalence of chronic hypertension in pregnancy in the United States is estimated to be as high as 3%. Women with chronic hypertension have an increased frequency of preeclampsia (17 to 25% vs. 3 to 5% in the general population), as well as placental abruption, fetal growth restriction, preterm birth, and cesarean section. The risk of superimposed preeclampsia increases with an increasing duration of hypertension.[1]

The World Health Organization and the American Diabetes Association define gestational diabetes mellitus (GDM) as "Any degree of glucose intolerance with onset or first recognition during pregnancy". GDM is a common condition affecting 0.6%-15% of all pregnancies each year, globally. In Pakistan, a study conducted in Karachi observed 8% prevalence of GDM.[2] Women with GDM are at risk of pre eclampsia (RR 1.94, CI 1.22–3.03) and their

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babies are at risk of macrosomia (RR 1.45, CI 1.06–1.95) and perinatal mortality (RR 1.59, CI 0.86–2.90).[3] The advanced maternal age, low monthly income, family history of diabetes, and obesity are the main significant risk factors for GDM. Early diagnosis of GDM is necessary to reduce maternal and fetal morbidity and to help to prevent or delay the onset of type 2 diabetes.[4] In the UK, it is recommended that an oral glucose tolerance test (OGTT), which is the diagnostic test for GDM, should be offered to women with any one of the following risk factors: body mass index (BMI)>30 kg/m^2, previous history of GDM or macrosomic baby (>4.5 kg), family history of diabetes or racial origin with a high prevalence of diabetes such as South Asian, African-Caribbean and Middle Eastern.[5]

A case control study found that during early pregnancy, women with pre hypertension had a small increased risk of GDM (odds ratio [OR] 1.56 [95% CI 1.16 –2.10]), and women with hypertension had a twofold increased risk of GDM (2.04 [1.14 –3.65]) compared with women with normal BP after adjusting for age, race/ethnicity, gestational week of BP, BMI, and parity. Thirty seven (9.7%) out of 381 cases were found hypertensive. Similar results were seen among the subset of women with BP levels measured before pregnancy (1.44 [0.95–2.19] for pre hypertension and 2.01 [1.01– 3.99] for hypertension).[6] A pilot study done in Sir Ganga Ram Hospital on total 40 pregnant women (20 pregnant women with chronic hypertension and 20 pregnant women without chronic hypertension),that found 3(15%) developed GDM out of 20 pregnant women with chronic hypertension and 1(5%) developed GDM out of 20 pregnant women without chronic hypertension. Pregnant women with chronic hypertension had history of hypertension of at least one year or more.

The risk factors of GDM and its complications are well known,[3,4,5] only one study provides evidence of chronic hypertension as risk factor for developing GDM.[6] We conducted this study in order to ascertain that presence of chronic hypertension in pregnancy may cause development of GDM. In this way prediction, early screening and prevention of GDM may be warranted to prevent the adverse outcomes of GDM along with control of hypertension for the prevention of its complications. The objective of this study is to determine whether chronic hypertension in pregnancy is associated with development of gestational diabetes mellitus. We hypothesized that there is an association between gestational diabetes mellitus and chronic hypertension in females presenting during second trimester of pregnancy.

METHODOLOGY

This case control study was conducted in the Department of Obstetrics & Gynaecology, Lady Aitchison Hospital, Lahore from July to December 2017. A total of 226 cases (113 in each group) (calculated with 80% power of test, 5% level of significance and taking expected percentage of chronic hypertension i.e. 12% in females with GDM and 12% in females without GDM) were included by non-probability consecutive sampling. Gestational diabetes mellitus was defined as oral glucose tolerance test with 100 grams glucose with two or more of the following after 24 weeks of gestation (on LMP): Fasting blood glucose 95mg/dl or more, blood glucose 180mg/dl or more after 1 hour of OGTT, blood glucose 155mg/dl or more after 2 hours of OGTT, blood glucose 140mg/dl or more after 3 hours of OGTT. Chronic hypertension of pregnancy was labeled if there SBP>140mmHg and DBP>90mmHg, diagnosed before pregnancy and using anti-hypertensive drugs. Females of age: 25 - 45 years of parity <5 presenting at Gestational age >24 weeks on LMP were included. Women with GDM were taken as cases while women without GDM were taken as control. Women with known history of diabetes mellitus prior to pregnancy (medical record), Women taking regular corticosteroids for more than two weeks (on medical record), Obese women with BMI>30 kg/m^2, Females who will have hypertension but unsure of hypertension before conception or no medical record available

were excluded. Informed consent and Demographic information (name, age, gestational age, parity) was obtained. These women were divided in two groups according to the operational definition i.e. case with GDM and control without GDM. Then BP of females was assessed and history of hypertension obtained. All information collected on a specially designed proforma. Data was entered and analysis through SPSS 22. Odds Ratio was calculated OR>1 was considered as risk and was taken as significant.

RESULTS

Table 1: Age of Patients (n = 226)

Age of pregnant woman	Frequency(n)	Percent
25-29 yrs	92	40.7%
30-35 yrs	108	47.8%
36-40 yrs	22	9.7%
41-45 yrs	4	1.8%
Total	226	100.0%

Table 2: Comparative analysis between Chronic Hypertension and Age of Pregnant Women (n = 226)

GDM			Chronic Hypertension		Total
			Yes	NO	
Exposed	**Age of pregnant woman**	25-29 yrs	2 (10%)	18 (90%)	20
		30-35 yrs	11(14.7%)	64(85.3%)	75
		36-40 yrs	5(31.2%)	11(68.8)	16
		41-45 yrs	1 (50%)	1(50%)	2
	Total		19(16.8%)	94(83.2%)	113
Un-exposed	**Age of pregnant woman**	25-29 yrs	1 (1.3%)	71(98.7%)	72
		30-35 yrs	3 (9.0%)	30 (91 %)	33
		36-40 yrs	1 (16.7%)	5 (83.3%)	6
		41-45 yrs	1 (50%)	1(50%)	2
	Total		6	107	113

DISCUSSION

This study showed that frequency of chronic hypertension among 226 women was 25(11 %) As study carried out by taking two groups one (n=113) who had GDM found to have chronic hypertension n=19(16.8%) and second was (n=113) who did not had GDM, only 6 women (5.3%) had chronic hypertension. In this study, women with chronic hypertension with at least history of five years with 20 weeks of gestation had one point 6 fold relative risk of developing GDM during pregnancy. A study among initially health women found high BP was associated with a twofold increased risk of developing type 2 diabetes during 4 years of follow-up after adjusting for known predictors of diabetes. Data on BP before or during pregnancy in relation to the occurrence of GDM are sparse. This study results are generally consistent with the one previous study of BP and risk of GDM.[6] Lao and Ho examined first-trimester BP and risk of GDM among 131 high-risk

Table 3: Comparative Analysis between Chronic Hypertension and Parity (n = 226)

GDM			Chronic Hypertension		Total
			Yes	NO	
Cases	**Parity**	Grand multipara 5 0r	7	21	28
		more	25%	75%	
		multipara 2-4	10	60	70
			14.2%	85.7%	
		primipara	2	13	15
			13.3%	86.7%	
	Total		19	94	113
			16.8%	83.2%	
Controls	**Parity**	Grand multipara 5 0r	2	18	20
		more	10%	90%	
		multipara 2-4	3	63	66
			4.5%	95.5%	
		primipara	1	26	27
			3.8%	96.2%	
		Total	6	107	113
			5.3%	94.7%	

Table 4: Comparative Analysis between GDM and Severity of Hypertension (n = 226)

	Chronic hypertension		Total
	Mild (low risk)	Severe (high risk)	
CASES	15	4	19
	79%	21%	100%
	5	1	6
CONTROL	83.3%	16.7%	100%
Odds ratio		3.57	
95 % CI		0.9542 to 3.8195	
P-value		P = 0.0676	

Chinese women and found that systolic BP above the median (109 mmHg) had a fourfold increased risk of GDM (OR 4.20 [95% CI 1.97– 8.94]). While the magnitude of the association they found was greater than our findings, they examined only high-risk women referred to a clinic providing antenatal care, categorized women according to a dichotomous cut off for systolic BP, and had limited information on confounders.

This study examined BP and GDM in women who underwent uniform screening for GDM. A clear definition of GDM was based on objective measures of pregnancy glycemia among a cohort with universal screening performed at 24 –28 weeks' gestation. Given the extensive chart review, we were also able to identify and exclude women with recognized preexisting diabetes before pregnancy. This study also has several limitations. During normal pregnancy, BP steadily decreases up to 21 weeks' gestation and then increases during the second half of pregnancy. Assessment of hypertension during pregnancy probably only captured severe case subjects in whom BP remained elevated even during early pregnancy. Other limitations of this study include the reliance on a single measure of BP, which may be influenced by external and internal stimuli, such as physical activity, diet, and emotional state. For the main analysis, we lacked information on smoking, a potential confounder; however. For the analysis of pregravid BP and GDM, data was missing information on BP on a large portion of unexposed subjects. We found the association between high BP and GDM was stronger among high age group and parity. There are several common pathogenic pathways to hypertension and GDM that may be underlying the association between the two conditions. Insulin resistance has been shown to be a contributing factor to both chronic and gestational hypertension, and it is known to be involved in the pathogenesis of GDM. Endo-thethial dysfunction has been found in women with GDM both during and after pregnancy and is also closely related to hypertension. Finally, markers of inflammation such as C-reactive protein have been associated with increased BP levels, and elevated early pregnancy CRP levels have been related to increased risk of GDM. In summary, this data suggest that women presenting with high BP, especially those who are increased age and parity, are at increased risk of developing GDM during pregnancy. Clinicians should be aware that this subgroup of women may warrant the initiation of early screening or dietary and exercise interventions to prevent there development of GDM.

CONCLUSION

There is significant association between chronic hypertension and gestational diabetes mellitus, all pregnant women with history of chronic hypertension should be tested or screened for gestational diabetes mellitus. So the prediction, early screening and prevention of GDM is warranted to prevent the adverse outcomes of GDM along with control of hypertension for the prevention of its complications

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COMPARATIVE STUDY OF ANTI-INFLAMMATORY EFFECT OF UNCARIA TOMENTOSA AND TORILIS LEPTOPHYLLA ON FREUD'S COMPLETE ADJUVANT INDUCED ARTHRITIS IN ANIMAL MODEL

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Abstract

Rheumatoid arthritis is a disease known to be progressive in nature and involving multiple systems of body. It is thought to be the result of an autoimmune response of the body, stimulated by external and also the genetic factors. It is characterized by synovial joints inflammation. A symmetric joint involvement and malformation is seen. Small joints of hands and feet are preferably affected by RA. RA also shows extra-articular and systemic manifestations. Extra-articular disease presents as uveitis, vasculitis, rheumatoid nodules, pericarditis and conjunctivitis. Expression of systemic involvement is in the form of anemia, fatigue and depression. There are many treatments like non-steroidal anti-inflammatory drugs (NSAIDs) and disease modifying anti-rheumatoid drugs (DMARDs) available for rheumatoid arthritis but up to 30% patients do not respond to these drugs. Herbal medicine and alternative medicine are considered to have least adverse effects and trend towards it is increased nowadays. Uncaria tomentosa, also known as cat's claw, is a plant used in traditional medicine, distributed in South America, mainly in Peru and Brazil as well as in Central America. There are various reports on U. tomentosa bioactivity, including anti-inflammatory and antioxidant properties, and protective effects against cancer, as well as positive effects in the cardiovascular, central nervous and locomotor systems. Cat's claw anti-inflammatory actions may be due to immunomodulation via suppression of NF kappa B, inhibition of inflammatory cytokines and suppression of TNF-a synthesis. On the other hand, Torilis leptophylla (T. leptophylla) also known as 'Chrikanger'. Jenus Torilis consists of a number of species found in North Africa, Asia and Europe. Essential oils extracted from the aerial parts of T. leptophylla possesses anti-inflammatory compound sesquiterpene hydrocarbons

Objective: To compare the anti- inflammatory effects of Uncaria tomentosa and Torilis leptophylla on inflammatory cells in blood.

Methodology: Adult, healthy, male Wistar albino rats weighing 140 ± 20 g were randomly divided into 4 groups of six animals each. Group I, II, III and IV by simple balloting method. Group II, III and IV rats were given subcutaneous FCA. Group I was given normal saline. Group II served as positive control (no treatment given). Group III and IV were treated with uncaria tomentosa bark and Torilis leptophylla whole plant extracts respectively.

Results: WBC count of Group I (Positive Control) were found significantly elevated ($P<0.001$) as compared to the control group. Treatments with UT and TLE extracts significantly decreased ($P< 0.05$ and $P < 0.01$ respectively) the WBC counts. Serum ALP levels were found significantly raised ($P < 0.001$) in diseased group (Group II) as compared to control group (Group I). Treatments with UT and TLE extracts significantly lessened ($P < 0.05$ and $P < 0.001$ respectively) the serum ALP levels as compared to diseased Group II. TLE extract showed better reduction of WBC count and serum ALP levels as compared to UT extract.

Conclusion: This study depicts that extracts of Uncaria tomentosa and T. leptophylla significantly decreased the white blood cell (WBC) count in blood and level of alkaline phosphatase in serum.

Key words: RA (Rheumatoid arthritis), UT (Uncaria tomentosa), TL (Torilis leptophylla), ALP (alkaline phosphatase), WBC (white blood cells), FDA (Freud's Complete Adjuvant)

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Rheumatoid arthritis (RA) is an autoimmune disease. It is characterized as chronic inflammatory condition that primarily affects joints. Inflammation caused by RA follows a progression of joint destruction leading to chronic pain, deformity and disability.[1]

RA is regarded with progressive non-specific signs and symptoms that include joint pain, swelling, redness, stiffness and reduced or very limited movement. A symmetric joint involvement and malformation is seen.[2] Small joints of hands and feet are possibly affected by RA.[3] In addition to joints RA also shows extra-articular and systemic manifestations. Extra-articular disease presents as vasculitis, rheumatoid nodules, pericarditis, uveitis and conjunctivitis.[2] Expression of systemic involvement in the form of anemia, fatigue and depression may also be present.[4]

Development of RA largely depends upon a multifaceted interaction among genetic and environmental aspects. Genetics contributes about 60% risk for RA Females are frequently affected as compared to males.[5] Prevalence of RA in Pakistan is 0.5% and disease is mainly polyarticular.[3]

Primary tissue affected by RA is synovial membrane of joints which gets inflamed. Inflammation caused by RA has a complex pathogenesis. Synovial inflammation is characterized by activation of macrophages, plasma cells, dendritic cells, T cells, B cells and angiogenesis. This process results in hyperplasia of membrane, fibrosis and formation of villi.[6]

Cytokines and chemokines are also produced by the stimulation of T cells and B cells. Macrophages cause formation of osteoclasts and cytokines such as IL-1, IL-6 and TNF-α.[7] These cytokines cause activation of genes that are responsible for inflammatory response in RA.

Due to the inflammation, membranes of neutrophils are stimulated and release free radicals and other reactive molecules such as hydroxyl radicals and hydrogen peroxide. Cytokines not only cause joint destruction but also have role in systemic manifestations of Ra.[8]

Several treatment options exist for the management of RA. These include pharmacological approach such as non-steroidal anti-inflammatory drugs (NSAIDs), glucocorticoids, disease modifying anti rheumatic drugs (DMARDs) and non-pharmacological approaches which include physical, occupational and psychological therapies.[9]

NSAIDs are widely used in the treatment of RA because they are highly effective in reducing the inflammation and pain associated with disease. DMARDs are considered to be the mainstay of treatment for Ra.[8]

These treatments are effective but have a variety of adverse effects. Prolonged use of NSAIDs is associated with upper gastrointestinal (GI) ulcers, bleeding, perforation and some cardiovascular risks. Similarly, use of DMARDs increases the possibility of malignancies, infections and immunologic abnormalities. Because of these drawbacks application of alternate treatment options is increasing.[10]

Nutraceutical preparations derived from animal and plant sources have been expended extensively for hundreds and thousands of years steadily to attain actual herbal medications which relieves pain and are befitting because of their comparatively fewer contrary effects.[11]

Uncaria tomentosa (panja bail) also known as 'Cat's Claw', belongs to the family Rubiaceae. The extracts of Uncaria tomentosa are frequently used in medicine of Peru, for the cure and management of arthritis, gastritis and for other inflammatory disorders.[12] Conventionally, the bark of cat's claw (UT) itself was consumed by natives to treat arthritis, bursitis and disorders of intestine even cancers of different kinds. Numerous analyses show that this Peruvian herb causes a generalized decrease in proinflammatory mediators and cytokines. Uncaria tomentosa possesses anti-inflammatory effect by preventing the initiation and stimulation of the transcriptional factor NF-κB. It also constrains the over expression of inducible genes allied with

inflammation[13]. It is evident that Uncaria tomentosa has anti-inflammatory effect in arthritis by inhibition of NF-κB and other mediators of inflammation for example IL-5 IL-6 and TNF- α.[12]

Similarly, Torilis leptophylla (T. leptophylla) belongs to the Apiaceae family, also known as Chrikanger. Jenus Torilis consists of a number of species found in North Africa, Asia and Europe. Phytochemical study of T. leptophylla demonstrated the presence of anthraquinones, terpenoids, alkaloids and cardiac glycosides.[14] Essential oils extracted from the aerial parts of T. leptophylla have been testified to contain anti-inflammatory compound sesquiterpene hydrocarbons.[15]

METHODOLOGY

Preparation of Animal

Adult, healthy, male Wistar albino rats weighing 140 ± 20 g were enrolled for the study. The animals were randomly divided into 4 groups of six animals each. Rats were kept in polypropylene cages having soft bedding, maintained at a temperature of 22 ± 2°C. Standard pellet feed and water ad libitum was served. Twelve hour light and dark cycle was maintained with relative humidity 40-70%.

Preparation of Ethanolic Extract of UT bark 100 grams of Uncaria tomentosa bark were extracted in 1L of absolute ethanol for 24 h at 37°C then the extract was centrifuged for 15 min at 4000 rpm. Supernatants were evaporated by vacuum centrifuge at low temperature for 1hr. Dry extract was re suspended in ethanol (1L) and stored at -20°C till further use.

Preparation of Methanolic Extract of TLE

Plant material was thoroughly washed and dried in shade for two weeks. Maceration of 500 g dried sample was done in 95% methanol for 48 hrs, with random stirring. Plant material was filtered and concentrated using rotary evaporator under reduced pressure at 37°C. The concentrated sample was freeze dried at - 44oC using lyophilizer and stored at 4°C till further use.

Induction of Arthritis Using Freund's Complete Adjuvant (FCA) Arthritis was induced to all groups of animals using FCA except group 1 which was non-arthritic. Group I was given sub plantar injection of 0.1 ml normal saline. FCA 0.1 ml was injected into sub plantar surface of left hind paw on day 1.[16]

FCA is composed of dry heat killed Mycobacterium tuberculosis 1 mg/ml. 17(Stills, 2005). Test samples and indomethacin were administered daily by oral route from day 12 till 28th day.

Day 1 Day 12 Day 29

Group I (n=6) (control) animals in group I served as control and were administered distilled water p.o. daily for 17 days. Group I was given sub plantar injection of 0.1 ml normal saline.

Group II (n=6) (positive control) animals in this group served as positive control and were given distilled water orally for 17 days.

Group III (UT Bark) (n=6) (UT 200 µg/ animal/ day) rats in this group were treated with Uncaria tomentosa bark extract at a dose of 200µg/ animal/ day orally for 17 days.

Group IV (n=6) (TLE 200 mg/kg) rats in this group were administered 200 mg/kg body weight of T. leptophylla extract daily by gavage for 17 days.

Blood Sampling

Determination of WBC in Blood

Blood was collected by cardiac puncture at 29th day and stored both in EDTA and serum vacutainers. Samples for whole blood were collected in EDTA tubes and placed in ice packs during sampling to avoid clotting. White blood cell (WBC) counts were measured using automated hematology analyzer.

Measurement of Serum Alkaline Phosphatase

Serum samples were collected in serum vacutainers containing blood clotting gel. Blood was allowed to clot for 1 hour and then centrifuged at 4000 r.p.m. for 5 minutes at 10°C18. Automated chemistry analyzer was used to measure serum alkaline phosphatase (ALP) of experimental rats.[19]

Statistical Analysis

The data was articulated as Mean ± S. D. Statistical analysis was performed using Statistical

Package for Social Sciences version 20. One way ANOVA was applied to observe the mean differences among control and experimental groups. Post hoc -Tukey test was used for comparisons. p- value of ≤0.05 was considered statistically significant. Microsoft Excel was used for graphical presentation of data.

RESULTS

Effect on WBC Count:

WBC count of Group II (Positive Control) was significantly (P<0.001) raised as compared to Group I (Control). Treatment with TLE and UT extracts significantly reduced the WBC count as compared to Group II (Positive Control). Reduction with TLE extract was more significant ($p < 0.01$) in comparison to the UT extract (P < 0.05).

Table 1: *Effect of UT and TLE extracts on WBC Count (103/µl).*

Groups	WBC Count (103/µl)
Group I (Control)	7.88 ± 0.12
Group II (Positive Control)	14.95 ± 0.23
Group III (UT)	12.62 ± 0.20
Group IV (TLE)	10.94 ± 0.25

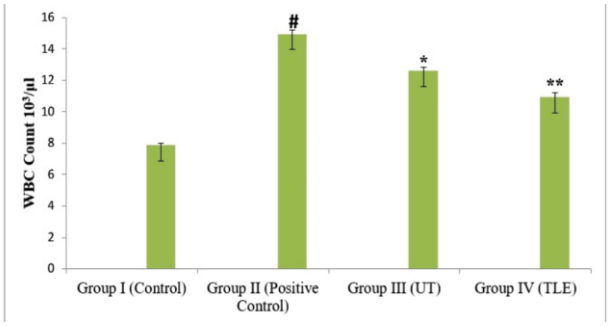

Fig. 1.1: *Effect of UT and TLE extracts on WBC count (10^3/µl)*

Serum ALP of Group II (Positive Control) was significantly (P<0.001) raised as compared to Group I (Control). Treatment with UT and TLE extracts caused significant reduction in serum ALP of Groups III (UT) and Group IV (TLE) as compared to Group II (Positive Control). Reduction with TLE extract was more significant ($p < 0.001$) in comparison to the UT extract (P < 0.05).

Table 2: *Effect of UT and TLE extracts on Serum ALP (U/L).*

Groups	Alkaline Phosphatase (U/L)
Group I (Control)	233.69 ±24.81
Group II (Positive Control)	553.28 ±26.49
Group III (UT)	429.04 ±21.40
Group IV (TLE)	325.87 ± 12.11

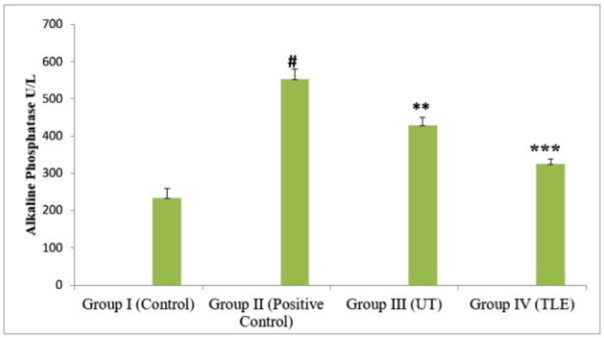

Fig 2.1. *Effect of UT and TLE Extracts on Serum ALP (U/L).*

DISCUSSION

Rheumatoid arthritis is a chronic disease caused by dysfunction of immune mechanisms. It results in damage to articular cartilage and bones along with reduced function.[20] Signs and symptoms of RA are non-specific and indefinite. These include pain, swelling, stiffness and redness of joints. Range of motion is also reduced. Uniformity is seen in joint involvement and deformity.[2]

A great number of treatment choices are available for the management of RA. These are pharmacological approach such as non-steroidal anti-inflammatory drugs (NSAIDs), disease modifying anti rheumatic drugs (DMARDs), glucocorticoids and non-pharmacological approaches which include psychological, physical and professional treatments.[9]

These treatment options are effective but have a lot of unwanted effects that reduce the patient compliance. Due to these and numerous other disadvantages use of alternative treatment options is growing.[10]

The extracts of Uncaria tomentosa are frequently used in medicine of Peru, for the cure and management of arthritis, gastritis and for other inflammatory

disorders.[12] Conventionally, the bark of cat's claw (UT) itself was consumed by natives to treat arthritis, bursitis and disorders of intestine even cancers of different kinds.[13]

Torilis leptophylla belongs to Apeacae family. Qualitative phytochemical study of T. leptophylla extracts and fractions demonstrated the presence of anthraquinones, terpenoids, alkaloids and cardiac glycosides. It has proven anti-inflammatory and anti-oxidant effects.[14]

Present study was planned to compare the effects of Uncaria tomentosa and Torilis leptophylla extracts in FCA induced arthritic rats. Two parameters WBC count and serum ALP were compared. Arthritis was successfully induced to Groups II, III and IV. Significant decrease was observed in inflammation and inflammatory cells by UT and TLE.

Group II (Positive Control) showed a significant ($p \leq 0.001$) elevation in WBC count and serum ALP as compared to Group I. Raised WBC count is a marker of increased inflammatory response to induction of arthritis. Exaggerated immune response is an important risk factor of arthritis. Alkaline phosphatase is a cytoplasmic enzyme. It is secreted by type II synovial cells. It indicates increased bone damage and remodeling.[19]

Treatment with UT and TLE significantly reduced WBC count in Groups III and IV. Reduction in WBC count was more significant ($p < 0.01$) in Group IV treated with TLE. This shows a better anti-inflammatory effect of TLE as compared to UT extract.

A significant reduction in serum ALP was observed in Group III (UT) and Group IV (TLE). Level of significance of group III (UT) was $p < 0.001$ while that of Group IV was $p < 0.05$. These values also show a better reduction of serum ALP by TLE.

Results of this study point towards anti-inflammatory effect of UT and TLE. Comparison of both plants shows a better reduction of inflammation by TLE. Anti-inflammatory effects of T. leptophylla can be attributed to the flavonoid and phenolic substances of the plant which have proven anti-inflammatory and anti-oxidant properties. Molecular basis for the mechanism of action of T. leptophylla requires further studies.

CONCLUSION

Outcome of this study illustrates that extracts of Uncaria tomentosa and T. leptophylla significantly decreased the white blood cell (WBC) count in blood. Moreover, the level of alkaline phosphatase in serum was also significantly reduced. However according to this research the extract of T. leptophylla was slightly more effective then uncaria tomentosa extract in reducing inflammation of joints in rats under observation of above mentioned parameters.

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Declaration of Interest

The authors declare that they have no competing interests.

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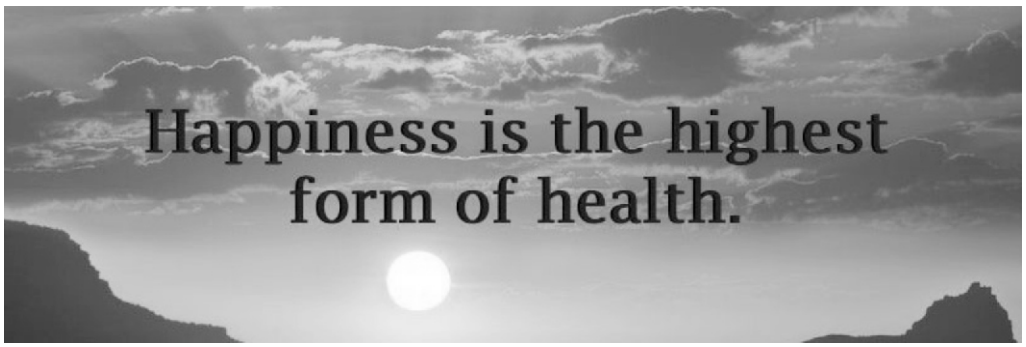

DETERMINANTS OF TREATMENT OUTCOME IN ADMITTED CHILDREN WITH SEVERE ACUTE MALNUTRITION IN A DISTRICT HEAD QUARTER HOSPITAL

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Abstract

Introduction: Malnutrition is one of the major problems of developing countries. It not only involves undernutrition but overnutrition as well. Malnourished children have a high mortality and morbidity when admitted in hospital. Several factors are responsible for that and it is very important that we know these factors beforehand for better outcome.

Objective: To assess the Determinants of treatment outcome in admitted children with severe acute malnutrition in a district head quarter hospital.

Study Design: Cross sectional study.

Place and Duration of Study: Department of Pediatrics, Children complex DHQ hospital Sheikhupura from 1st April 2018 to 31st October 2018.

Methods: A total of 196 children of either gender fulfilling the selection criteria were included in the study. Then clinical assessment including weight for height. Co morbidities, treatment given and outcome were recorded. All the information was collected through a specially designed proforma. Data were analyzed in SPSS version 20.The quantitative variable like age weight for height, co morbidities was presented as mean & standard deviation. The qualitative variable like gender and outcome was presented as frequency and percentage. p-value≤0.05 was declared as significant.

Results: Out of 198 patients 122(62.3%) were males while 76(38.38%) were female. The most common co morbidity associated with SAM were Anemia, decreased oral intake, fever, rickets, diarrhea and pneumonia. The mean age of patients was 20±0.5 months.139(70.7%) malnourished patients were improved, 14(7%) patients died, 27(13.77%) were moved to another hospital while 18(9.1%) failed to complete treatment. Variables showed that no fever (95% CI, P=0.047), Children without pneumonia (95% CI, P=0.001) Without rickets (95% CI, P=0.003) and without anemia (95% CI, P=0.041) had better outcome

The term malnutrition encompasses both over-nutrition and undernutrition. It is the single greatest threat to the survival of children. It is a global problem specially in underdeveloped countries leading to high mortality and morbidity. Approximately 55 million children suffer from acute malnutrition and they are under 5 years of age. On the otherhand 41 million children are overweight.

Severe acute malnutrition is the most extreme form of undernutrition. 19 million children die every year due to severe acute malnutrition. Half of these children live in South Asia and Sub Saharan Africa. It is defined as weight for height ratio of less than minus 3 standard deviations below the median reference range. Its prevention and treatment are fundamental for a child's development and healthy life.

Malnutrition is more than lack of food, it has multiple factors including poor care and feeding practices, insufficient energy, proteins and micronutrients, chronic diseases and incomplete vaccinations. According to the United Nations International Children Emergency Fund (UNICEF) 2018 data 149 million children are stunted 49.5 million are wasted and severe acute malnutrition affects 26 million.

Ethiopia is one of the countries affecting with

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severe acute malnutrition and having high childhood mortality rate. A study conducted in Ethiopia in 2017 showed that wasting, stunting, and underweight was 16.2% 43.1% and 24.8% respectively while the somali region figures were 27%, 38.4% and 38.8%. There were several factors affecting malnutrition. Diarrhea, receiving prelacteal feeding, and family size of 5 or above were positively associated with wasting. Male child, increasing age of child, and not fully immunized child were positive predictors for increasing stunting. Maternal illiteracy, male child, prelacteal feeding, and not fully immunized child were factors affecting underweight.

Another study done in west Ethiopia showed that anemia, fever, diarrhea, pneumonia and HIV are also associated with the treatment response. HIV is one of the important mortality factor in severely malnourished children in Africa ranging from 25% to 38% .There is lack of data of factors that effect malnutrition in our setup so its very important that we identify them and how drastically they can change outcome of malnutrition patients.

OBJECTIVE

To assess the Determinants of treatment outcome in admitted children with severe acute malnutrition in a district head quarter hospital.

METHODOLOGY

This was a cross sectional study conducted over a period of eight months from 1-04-18 to 31-10-18 in department of pediatrics, District head quarter Hospital Sheikhupura. Sample size of 198calculated with 95% confidence interval and 8% margin of error.

DATA COLLECTION AND ANALYSIS

198 children fulfilling the selection criteria were included in this study from admitted patients of Department of Pediatrics, District head quarter Hospital, Sheikhupura. An informed consent was obtained from parents of each child. Demographic profile (name, age, gender and contact) and was noted. Then children underwent clinical assessment including weight for height. Co morbidities, treatment given and outcome were recorded. All the information was collected through a specially designed proforma.

All the data was entered and analyzed through SPSS version 20. The quantitative variable like age, weight for height, co morbidities was presented as mean & standard deviation. The qualitative variable like gender and outcome was presented as frequency and percentage. p-value ≤ 0.05 was declared as significant.

RESULTS

Out of 198 patients 122(62.3%) were males while 76(38.38%) were female. (FIG 1) The most common co morbidity associated with SAM were Anemia, decreased oral intake, fever, rickets, diarrhea and pneumonia.(Table 1).The mean age of patients was 20±0.5 months.139(70.7%) malnourished patients were improved, 14(7%) patients died, 27(13.77%) were moved to another hospital while 18(9.1%) failed to complete treatment.(FIG 2). Variables showed that no fever (95% CI, P=0.047), Children without pneumonia (95% CI, P=0.001) Without rickets (95% CI, P=0.003) and without anemia (95% CI, P=0.041) had better outcome. (Table 2).

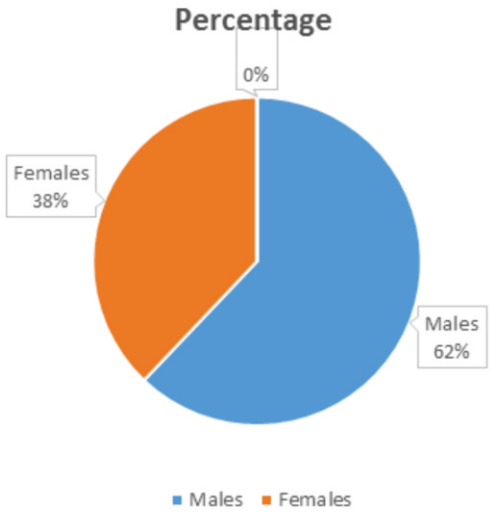

Fig 1: *Frequency Distribution of Gender*

Table 1: *Co morbidities distribution on treatment outcome.*

Co morbidities	Frequency (%)
Fever	72(36.7%)
Pneumonia	40(20.4%)
Rickets	86(43.8%)
Anemia	152(77.5%)
Diarrhea	68(34.7%)
Decrease oral intake	127(64.8%)

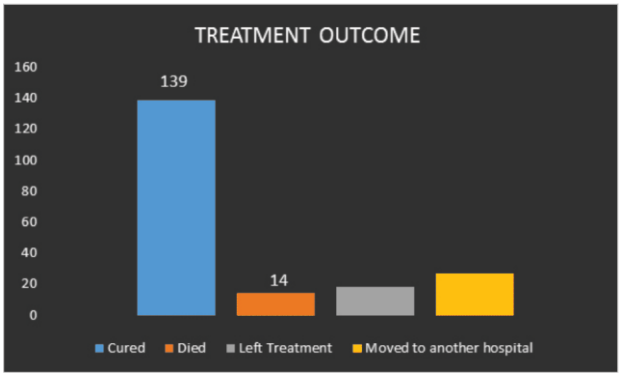

Fig 2: *Treatment outcome of admitted patients with severe acute malnutrition.*

Table 2: *Stratification of Determinants of Treatment Outcome of Severe Acute Malnourished Children*

Variables	P value
Fever (Not present)	0.047
Without pneumonia	0.001
Rickets (Not present)	0.041
Anemia (Not present)	0.003

DISCUSSION

This study showed that 70.7% of children with SAM were cured. This result was less as compared to study done in west Ethiopia by Muluken (2017) where 76% were cured. Similar results were seen in south Ethiopia (Wolaita, 92%). But the studies done in Zambia showed less cure rate(53.7). It could be because of multiple factors like inadequate treatment and treatment left by family.

Similarly, there are many determinants which effect the treatment outcome of children admitted with severe acute malnutrition. A study conducted in Yakatit 12 Hospital in Addis Ababa showed that of all the severely malnourished children (24.3%) have pneumonia, (11%) have tuberculosis, and (21%) have diarrhea. While in our study 20.4% have pneumonia and 34.7% have diarrhea.

Another study conducted in west Ethiopia showed that variables like fever, anemia, pneumonia and diarrhea were 38%, 71.2%, 21.5% and 35.1% respectively. According to their study fever didn't affect the treatment outcome but in our study it showed that a febrile children have a better outcome (p=0.047). The study conducted in Chad on data-analysis revealed that significant associations were found between not cured and diarrhea which was similar to our study.

There are still limitations to this study as the sample size was small and parental socio economic and educational status was not taken into account. However, it shows that factors and co morbid conditions associated with severe acute malnutrition are very important.

CONCLUSION

Outcome of severe acute malnutrition children in this study is better than many studies but it could still be improved if all the factors are taken into account. It will not only reduced mortality but improve the overall wellbeing of child.

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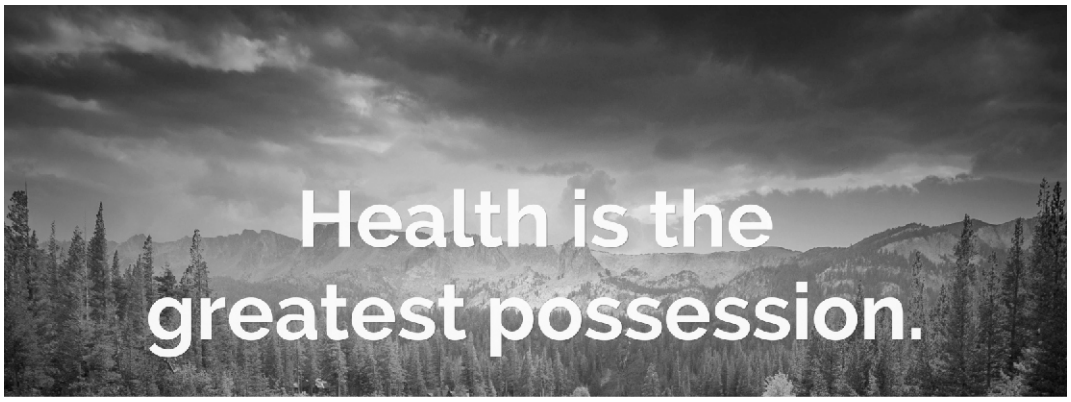

COMPARISON OF THE MEAN DURATION OF LABOUR AND MODE OF DELIVERY WITH AND WITHOUT EARLY AMNIOTOMY IN PRIMIGRAVIDA AT TERM

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Abstract

Objective: To compare the mean duration of labour and mode of delivery with and without early amniotomy in promigravidae at term.

Methodology: This randomized controlled trial was conducted in the Department of obstetrics and Gynaecology Unit II of Allama Iqbal Medical College, Jinnah Hospital Lahore from November 2012 to April 2013. Three hundred women fulfilling the inclusion criteria were enrolled in this study and they were admitted in labour room either from OPD or Emergency. Diagnosis of labour was made. The procedure of amniotomy was explained to all the patients. The cases selected were allocated randomly through lottery method into two groups. In Group A, amniotomy was done at cervical dilatation of 2.5 cm and Group B was expectantly managed group. Informed consent was taken from all the patients and likely benefits and risks of both the management were explain to the patients. Detailed History and examination including general physical obstetrical and sterile speculum examination was conducted in all the patients. Bishop score was assessed with sterile gloves in all patients and inferior pole of the membranes was ruptured by the Kocher's forceps in Group A. The amount and colour was noted. Vigilent fetal rate was monitored in all patients during labour. In Group B, membranes were kept intact as long as labour progressed smoothly. Rupture of membranes was done in Group B when there was arrest of dilatation as assessed by partogram and pelvic examinations. Total number of patients in group B, needing rupture of membranes before full dilatation was noted. All labour record was made on partogram ,with an alert line representing cervical dilataion of <1cm/hour and an action line drawn four hours to the right of alert line. Mean duration of labour and mode of delivery in terms of vaginal delivery, cesarean section due to failure to progress, fetal distressed was recorded.All the information was collected in specially designed proforma. Data was compiled, transferred and analyzed accordingly through SPSS (version 17). Means and standard deviations were calculated for quantitative data e.g. age, gestational age, and duration of labour. Frequency and percentage was calculated for mode of delivery. Chi square was applied for comparison of outcome variables i.e: Cesarean section and t test was used to compare the mean duration of labour in both groups. P value < 0.05 was considered as statistically significant.

Results: The study demonstrated that the length of all phases of labour was shorter in the group that had amniotomy as compared to control group with spontaneous labour (total length of labour= 9.92 versus 14.68 hours, p<0.01). Cesarean deliveries were increased in the amniotomy group (35 compared with 10 P < .001) due to failure to progress as well as fetal distress. On the other hand, neonatal outcome in terms of neonatal APGAR at 5 minutes was same in both groups(35 in each group p>0.05).

Conclusion: As compared with spontaneous labour, early amniotomy in labour is associated with more caesarean deliveries but shorter length of labour whereas neonatal outcome is unaffected.

Key words: Artificial rupture of membranes(ARM),active management, prolonged labour, Expectant management, amniotomy , ruptured membranes

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The rupturing of membranes in labour is a common practice[1]. Although an invasive procedure, many midwives and obstetricians regard it as straightforward and even insignificant[2]. At the point of transition from latent to active labour when the contractions are well in train and the cervix if fully effaced and dilated upto 3-4 cm., amniotomy if performed, causes subsequent labour is likely to be more efficient. Furthermore fetal surveillance is enhanced by opportunity to examine amniotic fluid directly for meconium or blood staining and by applying a fetal scalp electrode if desired. Requirements for analgesia are likely to be reduced because the increased efficiency of labour is reflected in its shorter duration.[4]

A study done of patients in spontaneous labour found membrane rupture to increase contraction frequency by 25% and intensity by 50%. In one trial it was proved that among nulliparous patients, the mean duration of active phase was 165 minutes in amniotomy group compared with 216 minutes in the control group. A 2nd trial showed mean labour duration was 4.9 hours in amniotomy group and 7.0 hours in the control group. There is no evidence that risk of neonatal asphyxia is increased among term infants exposed to a policy of early amniotomy.[7] On the other hand, Smyth et al's meta-analysis of the affect of amniotomy alone for the shortening of labour concluded that there was no evidence of any statistical difference in length of first stage of labour and that amniotomy was associated with increased risk of caesarean section1. In the four trials that reported on CTG abnormalities, there was evidence that these may be increased with amniotomy. As WHO suggests, when there is concern that labour is slowing down, benign measures to intensify contractions such as positional changes and movement may prevent the need for more invasive interventions[10]. There is little research comparing elective amniotomy with an intention to leave membranes intact until the second stage: only one study reports this intention[13]. In this trial 46% of the women allocated to non-intervention had their membranes ruptured at some stage.

According to Zhonghua Fu Chan KeZaZhi beneficial effects include reductions in labour duration and possible decrease in frequency of abnormal apgar score at one minute.[18] According to Cochrane database 2009 in prevention trials, early intervention with amniotomy and oxytocin appears to be associated with a modest reduction in the rate of caesarean section over standard care.[19] According to a randomized trial comparing a policy of early with selective amniotomy in uncomplicated labour at term, routine amniotomy may shorten the first stage of labour but not subsequent ones.[20] The objective of the study was to compare the mean duration of labour and mode of delivery with and without early amniotomy in promigravidae at term. Hypothesis of this study was that there is reduction in mean duration of labour in early amniotomy and an increase in cesarean delivery as compared to control group.

METHODOLOGY

This randomized controlled trial was conducted in the Department of obstetrics and Gynaecology Unit II of Allama Iqbal Medical College, Jinnah Hospital Lahore from November 2012 to April 2013. Three hundred cases in labour at term, who fulfilled the inclusion criteria, were induced in this study. These were divided into two groups, Group A and Group B with 150 patients each on random allocation basis, using random number table. Sample size was calculated with 80% power of test, 5% level of significance and taking expected percentage of c-section in both groups, that is 26% in amniotomy group and 12% in expectant group in primigravidae at term. Non probability purposive sampling was used. Patients with Gestational age >47 weeks (calculated by asking LMP), Primigravida with painful uterine contractions and cervical dilataion of 2.5 cm, Singleton pregnancy (on Ultrasound), Fetal head applied to the cervix were included. Patients having Vaginal bleeding, Major fetal abnormalities that are known at the time of admission. Pre-eclampsia, IDDM determined by history and appro-

priate laboratory tests were excluded. Amniotomy was defined as artificial rupture if membranes to facilitate labour ny doctor with amnihook at 2.5cm cerviacal dilatation. Duration of labour was defined as Length of time between onsent of regular pain-fuluterine contractions with cervical dilatation of 2.5 cm till the delivery of placenta. It was expressed as the number of hours. Mode of action was vaginal delivery, and Cesarean section is abdominal delivery of fetus. Caesarean section rate was taken as total number of cesarean section carried out and reasons for cesarean section like fetal distress, failure to progress, chorioamnionitis etc. and was compared in both study groups.

Three hundred women fulfilling the inclusion criteria were enrolled in this study and they were admitted in labour room either from OPD or Emergency. Diagnosis of labour was made. The procedure of amniotomy was explained to all the patients. The cases selected were allocated randomly through lottery method into two groups. In Group A, amniotomy was done at cervical dilatation of 2.5 cm and Group B was expectantly managed group. Informed consent was taken from all the patients and likely benefits and risks of both the management was explained to the patients. Detailed History and examination including general physical obstetrical and sterile vaginal examination was conducted in all the patients. Bishop score was assessed with sterile gloves in all patients and inferior pole of the membranes was ruptured by the Kocher's forceps in Group A. The amount and colour was noted. Vigilant fetal rate was monitored in all patients during labour. In Group B, membranes were kept intact as long as labour progressed smoothly. Rupture of membranes was done in Group B when there was arrest of dilatation as assessed by partogram and pelvic examinations. Total number of patients in group B, needing rupture of membranes before full dilatation was noted. All labour record was made on partogram, with an alert line representing cervical dilataion of <1cm/hour and an action line drawn four hours to the right of alert line. Mean duration of labour and mode of delivery in terms of vaginal delivery, cesarean section due to failure to progress, fetal distressed was recorded. All the information was collected in specially designed proforma.

Data was compiled, transferred and analyzed accordingly through SPSS (version 17). Means and standard deviations were calculated for quantitative data e.g. age, gestational age, and duration of labour. Frequency and percentage was calculated for mode of delivery. Chi square was applied for comparison of outcome variables i.e: Cesarean section and t test was used to compare the mean duration of labour in both groups. P value < 0.05 was considered as statistically significant.

RESULTS

During study period of six months, three hundred primigravidae between 37weeks to 40 weeks and 6 days gestation were admitted. Out of three hundered cases included in this study 150 subjects were included in amniotomy (Group A) and 150 were in control group B. The subjects were similar with respect to mean age and estimated gestational age at entry, p>0.05 (Table-I). All the subjects were followed till completion of data collection, nor did any subject dropped out. As will be shown later, 45 subjects under-went caesarean sections due to various reasons, hence the duration of labour in those patients was not calculated. The length of labour was significantly shorter in the case group with p <0.01. Percentage of cases delivered within 12 hours of labour in group-A was 50% while in group-B, it was 36.6 %. However, percentage of cases delivered between 12 to 24 hours of induction in group-A was 26% while in group-B, it was 50%. Only 10 cases of control group delivered after 24 hours i.e. 6.68%. So there was statistically significant difference in the duration of labour of both groups (Tables-II-V). In group-A, the percentage of normal vaginal delivery was found to be 46.67%, while in group-B, it was 76.67%. Instrumental delivery rate was 30 % in group-A and 16.67% in group-B. In group-A, rate of C-section was 23.33%

and in group-B 6.67%. The chi-square test indicates that there was significant difference in mode of delivery between two groups , p<0.01.(Table-V)

There were 15 patients with indication of fetal distress in group A while 5 patients in group B. There were 5 case of non-progress of labour in group A and 5 cases in group B. There were 15 cases of meconium in group-A as compared to group B with sponta-neous labour. No case of hyper stimulation of uterus and antepartum haemorrhage (APH) was noted in either group. Postpartum hemorrhage was noted in 3.33% cases of Group A and none of cases in Group B. There was a significant difference regarding maternal complications between two groups, p< 0.05. Passage of meconium was present in 10% in Group A and 3.33% in Group B. There was no significant difference in passage of meconium in both groups

Out of 30 babies of mothers in amniotomy group, only 3.33% had Apgar Score of 6 or less after 5 minutes and 23.31% had APGAR Score of 7 and 73% had APGAR score of 8 or more, while babies of mothers in control group,6.66% had Apgar Score of 6 or less, 16.6% had APGAR of 7 and 76.6% had 8-9. There was no significant difference between two groups as far as Apgar score at 5 minutes is concer-ned, p>0.05.. In group A 10% neonates were admi-tted to ICU and in group-B 20%. The chi-square test indicates a significant difference in both groups with respect to admission to ICU at 5% level of signifi-cance, p<0.0001.

Table 1: *Age Distrbution of Subjects Under Study (n=300)*

Age (Years)	Amniotomy Group (Group-A)		Spontaneous Labour (Group-B)	
	No. of patients	%	No. of patients	%
16-20	35	23.33	20	13.33
21-25	69	53.34	80	53.34
26-30	35	23.33	45	30
31-35	0	0	5	3.33
Total	150	100	150	100
Mean ± SD	23.50 ± 3.32		24.40 ± 3.47	

p > 0.05

Table 2: *Length of Labour (n=255)*

Length of Labour (hours)	Amniotomy Group (Group-A)		Spontaneous Labour (Group-B)	
	No. of patients	%	No. of patients	%
1-5	20	17.39	5	3.57
6-10	50	43.49	35	25
11-15	40	34.78	40	28.57
16-20	0	0	45	32.15
21-25	5	4.34	10	7.14
26-30	0	0	5	3.57
Total	115	100	140	100
Mean ± SD	9.92 ± 4.08		14.69 ± 5.29	

P < 0.01

Table 3: *Length Of 1st Stage Of Active Phase Of Labour (n=260)*

Length of labour (Hours)	Amniotomy group (Group-A)		Spontaneous labour (Group-B)	
	No. of patients	%	No. of patients	%
Up to 3 hours	35	30	15	10
3 – 6	55	48	75	52
6 – 9	25	22	45	31
10 – 12	0	0	10	7
Total	115	100	145	100
MEAN ± SD	3.97 ± 1.64		5.14 ± 2.58	

p < 0.05

Table 4: *Length of 2nd Stage of Active Phase of Labour (n=245)*

Length of labour Minutes	Amniotomy group (Group-A)		Spontaneous labour (Group-B)	
	No. of patients	%	No. of patients	%
Up to 30 minutes	75	68	95	70
31-60	30	27	35	26
61-90	5	5	5	4
Total	110	100	135	100
MEAN ± SD	37.00 ± 18.894		33.86 ± 16.26	

p > 0.05

Table 5: *Length of 3rd Stage of Active Phase of Labour (n=245)*

Length 3rd Stage (minutes)	Amniotomy Group (Group-A)		Spontaneous Labour (Group-B)	
	No. of patients	%	No. of patients	%
0-5	0	0	5	3.5
6-10	120	80	125	82.5
11-15	15	10	10	7
16-20	0	5	5	3.5
21-25	0	0	0	0
26-30	0	0	0	0
>30	5	5	5	3.5
Total	105	100	140	100
MEAN ± SD	14.57 ± 2.76		7.92 ± 4.2	

P < 0.001

Table 6: Mode of Delivery: (n=300)

	GROUP		Total
	CASE	CONTROL	
SVD	70	115	185
Cesarean section	35	10	45
Outlet Forceps	45	20	65
Ventouse	-	5	5
	150	**150**	**399**

Chi Square = 48 P-value = 0.001

DISCUSSION

Several points seem to be cleared from the available data. First early amiotomy of labour in nulliparous has shown to be related with decreased duration of labour as measured in terms of lengths of all phases of labour when compared with that of patients with spontaneous labour (9.92 hours versus 14.69 hours respectively, $p < 0.01$). This is in relevance to study conducted by Ayesha et al[70] who showed that women undergoing early amiotomy had shorter first stages of labour than women who were expectantly managed, whereas Incerti et al[71] reported that the total length of labour was longer in the early amiotomy group.

At one point where early amiotomy has shown to decrease length of labour in my study, there were 35 cases of emergency caesarean sections in females with early amiotomy in labour compared to that of 10 cases in spontaneous labour, ($p < 0.001$). This is similar to studies performed by F. Sahhaf et al.[72] Jeremey et al 73 who found a higher risk of cesarean associated with early amiotomy and F. Shoberi et al[74] also noted a higher risk of cesarean with early amiotomy group in the presence of an unfavorable cervix.

Number of instrumental deliveries was also higher in early amiotomy group than in spontaneous labour group (45 versus 20 respectively, $p<0.001$). Cheng et al 75 noted a similarly increased risk of instrumental delivery (odds ratio 1.09, 95% confidence interval 1.04-1.14).Various studies have also demonstrated this effect. [76,77,78]

Labour that has early amniotomy does result in higher satisfaction rates as compared to that following spontaneous onset[79]. The longer time delay between the start of the labour and the delivery in control group plays a significant part in this, with the mode of administration of the inducing agent, more vaginal examinations and the increase in caesarean deliveries being perceived as secondary issues.[80]

Regarding maternal morbidity, 5 patients in early amiotomy group experienced postpartum hemorrhage. This can be considered as insignificant bearing in mind that sample size in my study was not powered to evaluate these parameters adequately.

Neonatal outcomes were similar as regards to Apgar scores at 5 and 10 minutes in both groups (7 and 8 respectively). Hence it can be said that early amiotomy in labour did not bring about any adverse outcome in neonates.[81,82] Various studies demonstrated no change in the neonatal outcome similarly.

CONCLUSION

The success of augmentation in labour depends on the condition of cervix and in replicating as closely as the process of spontaneous parturition. Among the factors to be considered are the possibility of failed augmentatio and caesarean delivery, length of labour, cost and length of hospitalization and risk of maternal or neonatal infection. As care givers, our first priority is to do no harm. Given that, by definition, early amiotomy in labour provides no medical benefit to a woman or her child, we should only proceed with this intervention if the available evidence indicates that we will not incur additional risk to our patients

On the other hand, early amiotomy in labour has not been clearly shown to have detrimental associations for women with spontaneous labour, and it seems, for women with these characteristics who meet appropriate gestational age criteria, that early amiotomy of labour is an acceptable option for augmentation of labour.

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DEMOGRAPHIC & LIFESTYLE RISK FACTORS OF DYSGLYCEMIA IN HEPATITIS C PATIENTS

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Abstract

Objective: To determine the demographic and lifestyle risk factors of dysglycemia in hepatitis C positive patients in Mayo Hospital Lahore.

Methods: Acase control study was conducted atmayo hospital Lahore enrolling 96 (48: 48) Hepatitis C patients through purposive sampling. They were further divided into cases and controls on the basis of dysglycemia. Socio-demographic and life style risk factors data was collected through a pre tested questionnaire.Statistical analysis was done by using the SPSS version 26.

Results: There were 48(50%) male and 48(50%) females. Mean age was 44.41 ± 12.747 years. On bivariate analysis subject who aged > 40 years had 4.012 times higher chances of Dysglycemia(OR = 4.012). Males had 2.77 times higher chances of Dysglycemia than females.(OR = 2.77).50% cases had overweight/Obesity while only 29.2% controls had overweight / obesity.OR = 2.49 (C.I = 1.047 – 5.63, p-value 0.037).High fat diet, high carbohydrate diet, not performing exercise and regular smoking had significantly higher impact on Dysglycemia with Odd's ratio 2.69, 4.048, 2.57 and 3 respectively. Positive family history of diabetes (OR= 10.684) and stress (OR=7.22) had significant impact on dysglycemia.On multivariate analysis age (p= .016), employment status (p=.049), high fat diet (p=.042) and stress (p=.044) were associated with dysglycemia

Conclusion: Age, male gender, occupation, high BMI, smoking, high carbohydrate, high fat diet, family history and stress had significant relationship with dysglycemia.On applying binary logistic regression, we found final model with age, employment status, high fat diet and stress.

Keywords: Hepatitis C, glucose level, diabetes mellitus, glycemic control, life style and case control studies.

Viral infection with hepatitis C virus (HCV) is one of the main reason of liver disease and has significantly high tendency to be a reason of morbidity and mortality.[1] According to WHO 399,000 died due to HCV in 2016 and 71 million chronic carriers has been reported globally.[2] Developing countries have high prevalence including Pakistan with prevalence range of 3% to 7%, the second highest prevalence rate of hepatitis C.[3]

HCV infection is gradually recognized as an important reason for the extra hepatic manifestations and is known to be a major risk for the development of dysglycemia.4There is a rising epidemic of Dysglycemia worldwide. Dysglycemia is a metabolic disorder whose complications are quite high. Regarding pre-diabetes and diabetes mellitus(16.98%), burden of the disease is much higher now a days.[5]

In HCV infected patients dysglycemia may develop at any phase of disease. Numerous mechanisms have been described that includes Insulin resistance that develops due to interference with the insulin signaling pathways in the liver cells and production of cytokines, for instance, tissue necrosis factor alpha and interleukin 6 leads to increased inflammatory response and oxidative stress. [6]

Study reported that increasing age, weight above normal, and genotype 3 were the independent predictors of dysglycemia in patients infected with

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HCV.6Naing C et al found that Hepatitis C positive subjects were at an increased risk of developing dysglycemia compared to uninfected controls. Among hepatitis C cases male gender and older age had an increased frequency of dysglycemia.[7]

The rationale of our research is that dysglycemia and HCV infection are prevalent diseases, with a high impact on health, and have long been considered to be biologically linked. The prevalence of dysglycemia in HCV positive subjects is expected to be double or even triple the number in the normal population. A large amount of studies described the effects of HCV infection on the onset, progression, and severity of diabetes. However demographic and life style risk factors accountable for dysglycemia were not directly investigated. By this study high risk groups were identified and preventive strategies may be planned accordingly. The objective of this study was to determine the demographic and lifestyle risk factors of dysglycemia in hepatitis C positive patients in Mayo Hospital Lahore.

METHODOLOGY

A case control study conducted at mayo hospital Lahore, from 1-05-2015 to 30-04-2016. Calculated sample size was 96 (48 cases, 48 controls) at 95% confidence interval and 80% power of the test. Institutional Review Board gave permi-ssion to conduct this research. Diagnosed Hepatitis C patients (PCR Positive) were enrolled in the study by non-probability purposive sampling technique. Informed consent was obtained from all the subjects. Fasting blood glucose level was measured and subjects were divided into cases and controls according to their glycemic status till 48 cases and 48 controlled were enrolled. Cases were dysglycemic whereas controls had normal glucose level. Patients who were on interferon therapy, had hepatitis B or end stage renal disease were excluded from the study along with pregnant females. They were interviewed, examined &data was recorded in a pre-structured and pretested questionnaire. Questionnaire contained questions regarding demographic and life style risk factors of dysglycemia. Dysglycemia was determined by measuring fasting blood glucose. Operational definitions are given below:

Dysglycemia included Hyperglycemia > 126 mg/dl and impaired fasting glucose 100 to 126 mg/dl. A Person is considered illiterate who cannot read or write paragraph (3 lines) in national/regional language with comprehension."A smoker is a person who has smoked at least 100 cigarettes and now smokes at least one cigarette every day. Sedentary life style is the lifestyle in which more time is spent while sitting on computers, televisions or in inactive job, sitting position in office/ house ≥9 hours excluding sleep time. For determining stress, Perceived stress scale was used. Score 21 and above was taken as stress presence. Lack of exercise was defined as not performing aerobic activity for at least 30 minutes per day, five times a week. "Body mass index (BMI) was calculated by weight in kg divided by square of the height in meters." Where Obesity was considered when BMI was 30 kg/m^2 or more and overweight was labeled whenBMI was 25 to 29.9 kg/m^2. A daily diet whose more than 65% calories are obtained from carbohydrate. A daily diet whose more than 35% calories are obtained from fat, 24 hours dietary history and standard food composition table 8 was used for this purpose.

Statistical analysis was done by using the SPSS (software package for statistical analysis) version 26. All variables were described by using frequency percentages. The quantitative variables, age and body mass index were analyzed by mean and standard deviation. The qualitative variables like gender, occupation, education, marital status, high fat diet, high carbohydrate diet, smoking, lack of exercise, overweight, obesity, sedentary life style, house hold composition, family history of diabetes mellitus and stress were analyzed by calculating ODD's ratio and Chi-square test (Bivariate Analysis). Confounders were controlled by binary logistic regression analysis (Multivariate Analysis). P value < 0.05 was considered significant.

RESULTS

In this study mean age of subjects was 44.41 ± 12.747 years. According to age groups 47.91% subjects were ≤ 40 years of age while 52.08% subjects were > 40 years of age. There were 48(50%) male and 48(50%) female subjects. In cases mean age of patients was 49.21 ± 12.492 years and in controls mean age of patients was 39.60 ± 11.19 years. Statistically mean age of cases was higher as compared to control group with p-value < 0.001.

Bivariate Analysis by Chi square, Odds Ratio & 95% CI:

When data was stratified over age (at 40 years) we found significant higher odds ratio (OR = 4.012) that means there were 4.012 times higher chances of Dysglycemia for those aged > 40 years. Moreover for males there were 2.77 times higher chances of Dysglycemia when compare to females (OR = 2.77) and married subjects had insignificant but 2.2 time higher chances of Dysglycemia.

Most of the subjects (60.42%) had normal weight, while 31(32.29%) subjects were overweight and rests of 7(7.29%) subjects were obese. Mean BMI in cases and controls was 25.477 ± 3.814 and

Table 1: *Bivariate Analysis of the Risk Factors of Dysglycemia in Hcv Patients*

VARIABLE	CATEGORIES	CASES (HCV & DYSGLYCEMIC)	CONTROLS (HCV & NORMOGLYCEMIC)	X^2 (P VALUE)	ODDS RATIO (95% CI)
Age Groups	> 40	33(68.8%)	17(35.4%)	10.68 (0.001)	4.012 (1.72 – 9.39)
	< 40	15(31.2%)	31(64.6%)		
Gender	Male	30(62.5%)	18(37.5%)	6 (0.014)	2.77 (1.261 – 6.34)
	Female	18(37.5%)	30(62.5%)		
BMI	Over weight/ Obesity	24(50%)	14(29.2%)	4.35 (0.037)	2.42 (1.047 – 5.63)
	Normal	24(50%)	34(70.8%)		
Marital status	Married	44(91.7%)	40(83.3%)	1.52 (0.217)	2.200 (0.615 – 7.868)
	Unmarried	4(8.3%)	8(16.7%)		
Education of patients	Uneducated	15(31.2%)	12(25%)	0.46 (0.496)	1.36 (0.558 - 3.334)
	Can read or write	33(68.8%)	36(75%)		
Employment Status	Working (employed)	29(60.4%)	15(312%)	8.22 (0.004)	3.358 (1.448 – 7.785)
	Non-working	19(39.6%)	33(68.8%)		
Residence	Rural	21(43.8%)	22(45.8%)	0.042 (0.837)	0.919 (0.441 – 2.055)
	Urban	27(56.2%)	26(54.2%)		
High fat diet	Yes	24(50%)	13(28.3%)	5.32 (0.021)	2.69 (1. 149 – 6.310)
	No	24(50%)	35(76%)		
High carbohydrate diet	Yes	30 (62.5%)	14(29.2%)	10.74 (0.001)	4.048 (1.724 – 9.505)
	No	18 (37.5%)	34(70.8%)		
Not doing exercise	Yes	27(56.2%)	16(34.7%)	5.09 (0.024)	2.57 (1. 124 – 5.884)
	No	21(43.8%)	32(69.5%)		
Sitting > 9 hours	Yes	19(39.6%)	16(33.3%)	0.405 (0.525)	1.31 (0.569 -3.016)
	No	29(60.4%)	32(66.7%)		
Regular Smoking	Yes	18(37.5%)	8(16.7%)	5.27 (0.022)	3.00 (1.15 – 7.8)
	No	30(62.5%)	40(83.3%)		
Obesity/Overweight	Yes	24(50%)	14(29.2%)	4.35 (0.037)	2.42 (1.047 – 5.63)
	No	24(50%)	34(70.8%)		
Family system	Joint family	27(56.2%)	30(62.5%	0.389 (0.533)	0.771 (0.341 – 1.745)
	Nuclear family	21(43.8%)	18(37.5%)		
Family history of Diabetes	Yes	29(60.4%)	6(12.5%)	23.78 (0.0001)	10.684 (3.8 – 30.006)
	No	19(39.6%)	42(87.5%)		
Stress	Yes	30(62.5%)	9(18.8%)	19.04 (0.0001)	7.22 (2.847 – 18.32)
	No	18(37.5%)	39(81.2%)		

23.61 ± 2.67 respectively, significantly higher mean BMI was observed in cases when compared to control group and p-value was less than 0.001. A total of 50% cases had overweight/Obesity while only 29.2% controls had overweight / obesity in this study. According to odds ratio we found significant higher risk of Dysglycemia in cases when compared to control i.e. OR = 2.49 (C.I = 1.047 – 5.63, p-value 0.037). Table I

In this study education and residential status had no significant impact on Dysglycemia and employment status of the subjects had significant higher impact on Dysglycemia (OR = 3.358). Table I

High fat diet, high carbohydrate consumption, no. exercise and regular smoking had significantly higher impact on Dysglycemia with ODD's ratio of 2.69, 4.04, 2.57 and 3 respectively. On the other hand sitting ≥9 hours had higher impact on Dysglycemia but this impact was not significant, p-value > 0.005.Table I

When no. of cigarettes per day were analyzed, no significant difference between cases and control group was seen, as mean no. of cigarettes smoked in cases and controls was 9.18 ± 5.334 and 8.12±5.540, p-value > 0.620. In this study joint family system had no impact while family history of diabetes and stress of patients had significant impact on Dysglycemia. There are 10.684 times more chances of Dysglycemia for those who had positive family history of diabetes and 7.22 times more chances of Dysglycemia for those who had stress. Table I

Multivariate Analysis by binary logistic regression:

All variable that had significant impact in bivariate analysis were processed for binary logistic regression to control confounders and get the final result. We found final model with age, employment status, high fat diet and stress. From table we can see that these parameters had significant p-value. Table II

Table 2: Multivariate Analysis of the Risk Factors of Dysglycemia in Hcv Patients by Applying Binary Logistic Regression

Variables	P value	ODD's ratio	95% CI	
			upper	lower
Age>40	.016	4.439	1.327	14.850
Employment status	.049	7.272	1.012	52.281
High fat diet	.024	4.418	1.221	15.987
Stress	.044	3.385	1.034	11.082

DISCUSSION

In current study mean age of cases was 49.21 ± 12.492 years and in controls mean age of patients was 39.60 ± 11.19 years. When data was stratified over age (at 40 years) we found significant higher odds ratio (OR = 4.012) that means there were 4.012 times higher chances of Dysglycemia for those aged > 40 years. Statistically mean age of cases was higher as compared to controls, p-value < 0.001. In a study Old Asian patients were 3.7 times more prone to have dysglycemia than younger HCV patients, while the risk was lesser among non-Asian HCV patients.9Few other studies supported our findings too.[10,11]

A study reported no significant difference of gender, percentage of male gender was 65.5% and 75% in diabetic and non-diabetic HCV patients respectively while there were 34.5% and 25% females in diabetic and non-diabetic HCV patients. 12 But in current study, for males there were 2.77 times higher chances of Dysglycemia when compare to females, (OR = 2.77). So our results are different than above cited study. In another study male members had more chances to develop dysglycemia than female participants in both Asian as well as non-Asian population. These results are similar to the present study.[10,12]

In current study married subjects had insignificant but 2.2 times higher chances of Dysglycemia while education level had no significant impact on dysglycemia. In a study education level and marital status of the patients had insignificant relation with the presence of diabetes among HCV patients that is in accordance with our study.[13]

We found mean BMI in cases and controls was 25.477 ± 3.814 and 23.61 ± 2.67 respectively, mean BMI was significantly higher in cases when com-

pared to control group and p-value was < 0.001. A total of 50% cases had overweight/Obesity while only 29.2% controls had overweight / obesity in this study. According to odds ratio we found significant higher risk of Dysglycemia in cases when compared to control i.e. OR = 2.49 (C.I = 1.047 – 5.63, p-value 0.037). Residential status had no significant impact on Dysglycemia in our study. Similar findings were present in other studies. Residence in urban areas was associated with the development of diabetes among HCV patients in a study.[10,13,14]

Working (employed) subjects had significant higher impact on Dysglycemia (OR=3.358). Abdelaziz et al found that employment status was a significant risk factor for the presence of dysglycemia in HCV patients. Skilled workers had more chances to develop diabetes.[13,14]

A healthy lifestyle is important for patients of HCV that includes physical activity. Physical activity may be in the form of brisk walk, jogging cycling or others, moderate in intensity and must be performed for 30 minutes for 3 to 7 days a week. The patients with HCV and restricted physical activity are at higher risk of Dysglycemia. Current study supported this finding. On the other hand sitting ≥ 9 hours had higher impact on Dysglycemia with OR = 1.31 but this impact was not significant, p-value = 0.525. Regular smoking had a significantly higher impact on dysglycemia with ODD's ratio 3 and p value 0.022.When no. of cigarettes per day were analyzed no significant differences between cases and controls was seen, as mean no. of cigarettes in cases and controls was 9.18 ± 5.334 and 8.12 ± 5.540 , p-value > 0.620. In another study of HCV patients dysglycemia was found almost in equal proportions among smokers and non-smokers with p=0.69.15 In an Egyptian study 62.7% diabetic HCV subjects gave history of cigarette smoking whereas 37.3% non-diabetic HCV subjects smoked and smoking was found to be a predictive factor in the association of dysglycemia and HCV infection.[10,14]

Diet plays an essential role for HCV patients. Diet high in energy is usually recommended for such patients. Energy needs per unit body mass of patients of HCV infection are high both in the presence or absence of cirrhosis as compared to healthy individuals.[16] Liver plays a vital role in the metabolism of carbohydrates and blood glucose levels regulation. When functions of liver are impaired due to any disease of the liver, glucose homeostasis is often disturbed.[17] In the present study we found high carbohydrate and high fat consumption has significantly higher impact on Dysglycemia i.e. OR = 2.69 and 4.048 respectively.[17] In a study high fat levels were associated with dysglycemia.[10]

In this study family system had no impact while family history of diabetes has strong impact. There are 10.684 times more chances of Dysglycemia for those who had positive family history of diabetes. Abdelaziz et al and Hashim support our findings.[11,13]

In the current study Stress of patients had significant impact on Dysglycemia and 7.[22] times more chances of having Dysglycemia for those who had stress. High prevalence of mental illness among HCV was reported in a previous study.[18] Another study supported association between different forms of stress and diabetes.[19]

On applying logistic regression we found final model with age, occupation, high fat diet and stress. All parameters had significant p-values and Odds ratios. Older age and positive family history of diabetes were the only independent risk factor for diabetes type 2 in HCV positive patients in a study. These findings are similar to our findings for age and inconsistent to our other findings.[13,14]

CONCLUSION

In this study significantly higher risk of Dysglycemia was found among HCV patients who were aged >40 years, male patients, had raised BMI, married, working (employed), regular smokers, consumed high carbohydrate & high fat diet, positive family history of diabetes or had stress. On applying binary logistic regression we found final model with age, employment status, high fat diet and stress.

Limitations

Single center, Small sample size, case control study design (Recall Bias), Non probability Sampling.

Recommendations

In future patients with HCV must be motivated to control their modifiable risk factors and should be prevented for dysglycemia to avoid incidence of diabetes mellitus. Preventive strategies should be applied specially to those who are at high risk. No doubt if patients with HCV develop Diabetes mellitus then they at higher risk of mortality and other complication related to HCV and diabetes.

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EFFICACY OF OLOPATADINE HCL 0.1% OPHTHALMIC SOLUTIONS IN ALLERGIC CONJUNCTIVITIS

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Abstract

Objectives: To determine the efficacy of Olopatadine HCL 0.1% ophthalmic solutions in allergic conjunctivitis.

Methods: This descriptive case study was carried out over a period of six months in department of Ophthalmology, Jinnah hospital Lahore. A total of 150 cases fulfilling the inclusion/exclusion criteria coming to Department of Ophthalmology, Jinnah Hospital, Lahore were enrolled. Every patient was treated with Olopatadine HCL 0.1% BD and assessed clinically at 7th day of follow-up. The efficacy of the drug was recorded according to operational definition by the researcher himself. Presence/absence of conjunctivitis was recorded.

Results: In our study, 26%(n=39) were between 10-30 years of age and 74%(n=111) were between 31-60 years, mean±SD was calculated as 35.55+10.49 years. 35.33%(n=53) were males and 64.67%(n=97) were females. The efficacy of olopatadine HCL 0.1% ophthalmic solutions in allergic conjunctivitis was recorded in 55.33%(n=83) while in 44.67%(n=67), no findings of efficacy were recorded.

Conclusion: We concluded that the frequency of efficacy of Olopatadine HCL 0.1% ophthalmic solutions is higher among patients. So, it is recommended that every patient who presents with allergic conjunctivitis, may be managed with this drug. However, it is also required that every setup should have their surveillance in order to know the frequency of the efficacy of the drug.

Keywords: Allergic conjunctivitis, Management, Olopatadine HCL 0.1% ophthalmic solutions, Efficacy

Allergic conjunctivitis is a relatively benign ocular disease that causes significant suffering and use of healthcare resources, although it does not threaten vision. Ocular allergy is estimated to affect at least 20 percent of the population on an annual basis, and the incidence is increasing.[1] It is speculated that environmental factors are essentially responsible for this increase.[2]

The most prominent symptoms of allergic conjunctivitis include itching, tearing, foreign body sensation and photophobia.[3-4] The most prominent signs include crusted eyelids that are often matted shut, especially after sleep, hyperemia and either watery or mucoid discharge from one or both eyes, but no loss of visual acuity.[5] This presentation usually makes the diagnosis straightforward; however, most family physicians recognize the difficulty in clinically differentiating a viral from a bacterial infection.[6]

For the management of conjunctivitis, several local ocular drugs, such as antihistamines, anti-allergic agents, and corticosteroids, have been developed as commercially available eye drops recently.[7-8] Olopatadine hydrochloride exerts a wide range of pharmacological actions such as histamine H1 receptor antagonist action, chemical mediator suppressive action, and eosinophil infiltration suppressive action.[9]

In a study conducted by Aguilar AJ[10], positive clinical results were observed in 80% to 87.5% of treated patients but it is not clear what the term 'positive clinical results' implies. The term does not clarify the 'relieve' or 'absence' of symptoms and signs. Since this study does not give results in clear

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measureable terms so we assume that the efficacy will be present in 60% of patients. The rational of this study is to clarify this ambiguity and to generate the results in our population as there is no local study present.

METHODOLOGY

This descriptive case series was conducted in department of Ophthalmology, Jinnah Hospital, Lahore from 11-11-2013 to 11-05-2014. Total 150 patients were enrolled in the study. Inclusion criteria was the age between 10-60 years, both gender and all cases of allergic conjunctivitis presented in OPD. Exclusion criteria included patients who were already under treatment of allergic conjunctivitis (on history and medical record) and patients having known allergy for olopatadine HCL 0.1%(on history and medical record)

The allergic conjunctivitis was determined on clinical examination having symptoms and signs of itching, tearing, hyperemia and mucoid discharge. Every patient was treated with Olopatadine HCL 0.1% twice a day and assessed clinically at 7th day of follow-up, then the efficacy of the drug was recorded.

The efficacy was defined as the absence of symptoms and signs of allergic conjunctivitis on 7th day after the instillation of Olopatadine HCL 0.1% twice a day.

Informed consent of the patients was obtained to include their data in the study. Demographic profile, age, gender was recorded. Patients showing no efficacy were managed according to depart-mental protocols.

The data was analyzed through SPSS version 16. Mean and SD was calculated for age. Frequency and percentage was calculated for categorical variable i.e. gender and efficacy i.e. absence of allergic conjunctivitis. Stratification for age and gender was done to control the effect modifiers. No test of significance was required as the study is descriptive.

RESULTS

A total of 150 cases fulfilling the inclusion/ exclusion criteria were enrolled to determine the efficacy of Olopatadine HCL 0.1% ophthalmic solutions in allergic conjunctivitis. Age distribution of the patients was done which shows that 26% (n=39) were between 10-30 years of age and 74% (n=111) were between 31-60 years, mean±SD was calculated as 35.55 ± 10.49 years (Table No. 1). Gender distribution of the patients was done which shows that 35.33%(n=53) were males and 64.67% (n=97) were females(Table No. 2).

Efficacy of olopatadine HCL 0.1% ophthalmic solutions in allergic conjunctivitis was recorded in 55.33% (n=83) while 44.67%(n=67) had no findings of efficacy(Table No. 3).

Stratification for efficacy of olopatadine HCL 0.1% ophthalmic solutions in allergic conjunctivitis with regards to age shows that out of 83 effectively treated cases, 16 were between 10-30 years and 67 were 31-60 years of age(Table No. 4).Stratification for efficacy of olopatadine HCI 0.1% ophthalmic solutions in allergic conjunctivitis with regards to gender shows that out of 83 effectively treated cases, 31 were males and 52 were females(Table No. 5).

Table 1: *Age Distribution (n=150)*

Age (in years)	No. of patients	%
10-30	39	26
31-60	111	74
Total	**150**	**100**

Mean ± SD: 35.55±10.49

Table 2: *Gender Distribution (n=150)*

Gender	No. of patients	%
Male	53	35.33
Female	97	64.67
Total	**150**	**100**

DISCUSSION

Around 15-20% of the population worldwide is affected by seasonal allergic conjunctivitis (SAC) which occurs from type 1 allergic reactions.[11,12,13,14] The most common symptom of SAC is ocular itching. In addition, conjunctival redness, tearing,

mucus discharge, chemosis and lid edema are other common symptoms of SAC. Mast cells play an important role in the pathogenesis of SAC.[15] The basic principle of treatment is keeping a patient away from allergic agents. However, this treatment approach does not often work because most allergic agents are in the air.[16]

Table 3: Efficacy of Olopatadine HCL 0.1% Ophthalmic Solutions in Allergic Conjunctivitis. (n=150)

Efficacy	No. of patients	%
Yes	83	55.33
No	67	44.67
Total	**150**	**100**

Table 4: Stratification for Efficacy of Olopatadine HCL 0.1% Ophthalmic Solutions in Allergic Conjunctivitis with Regards To Age. (n=150)

Age (in years)	Efficacy	
	Yes	No
10-30	16	23
31-60	67	44

Table 5: Stratification for Efficacy of Olopatadine HCL 0.1% Ophthalmic Solutions in Allergic Conjunctivitis with Regards to Gender. (n=150)

Gender	Efficacy	
	Yes	No
Male	31	22
Female	52	45

We planned this study to clarify the ambiguity regarding efficacy of Olopatadine HCI for the management of allergic conjunctivitis and to generate the results in our population as there is no local study present.

In our study, 26%(n=39) were between 10-30 years of age and 74%(n=111) were between 31-60 years, mean±SD was calculated as 35.55±10.49 years, 35.33%(n=53) were male and 64.67%(n=97) were females. Efficacy of olopatadine HCI 0.1% ophthalmic solutions in allergic conjunctivitis was recorded in 55.33%(n=83) while 44.67%(n=67) had no findings of efficacy.

We found similarity of our results regarding age and gender with Abdullah FE[17] who identified the etiological agent in bacterial conjunctivitis who recorded a high frequency of conjunctivitis among females 61% (n=122) and rest were males 39% (n=78). The majority of cases were noted between 41 to 70 years (79.22%) similar to the findings of our study.[17]

Aguilar AJ[10] compared the clinical efficacy and tolerance of 0.1% olopatadine hydrochloride (OHC) versus 0.05% ketotifen fumarate (KF) in the management of allergic conjunctivitis and recorded that clinical improvement of the signs and symptoms of allergic conjunctivitis occurred in 42.5% to 62.5% of the patients in Group A when assessed at 30 min following the first topical ocular dose of olopatadine. They concluded that olopatadine hydrochloride controlled allergic conjunctivitis symptoms and signs more rapidly and to a greater extent than ketotifen fumarate and our findings clarify the above findings.

Another study by Spangler DL[18] compared the efficacy of olopatadine hydrochloride versus azelastine hydrochloride and placebo (artificial tears) in the conjunctival allergen challenge (CAC) model and that olopatadine was significantly more effective than azelastine in the management of itching associated with allergic conjunctivitis in the CAC model.

Butrus S and workers[19] compared the clinical efficacy and comfort of olopatadine with those of nedocromil in the conjunctival allergen challenge model, they found that in the conjunctival allergen challenge model, olopatadine was more efficacious and comfortable than nedocromil in reducing the itching associated with allergic conjunctivitis.

Shah-Jalal Sarker and others[20] studied whether 0.1% olopatadine hydrochloride (OHCL) is more effective and safer than 0.025% ketotifen fumarate (KF) in the management of allergic conjunctivitis, they recorded that both drugs reduced signs and symptoms of allergic conjunctivitis at 2 weeks from baseline. The treatment with 0.1% OHCL was more effective compared with 0.025% KF, as the mean (SD) composite score of 6.3 (±1.3) for the OHCL group was significantly higher than that of 4.3 (±1.7) for the KF group ($p < 0.001$, two-sided t-test). KF reduced the mean scores of hyperemia, tearing,

itching and photophobia by 64, 63, 55 and 81%, respectively, while OHCL reduced these by 96, 97, 88 and 96%. Relative significant efficacy was achieved for hyperemia, tearing and itching ($p \leq 0.001$) but not for photophobia ($p = 0.315$). No adverse events were observed in the OHCL group while 30% of patients in the KF group showed mild stinging or foreign body sensation after instillation of the first dose and concluded that 0.1% OHCL is more effective and safer (in the short term) than 0.025% KF in the management of allergic conjunctivitis. Comparing the results of our study with other studies clarifies that the efficacy of Olopatadine HCL 0.1% ophthalmic solutions in allergic conjunctivitis is higher, however, our findings are primary in our local population, some other trials are required to authenticate the current findings.

CONCLUSION

We concluded that the frequency of efficacy of Olopatadine HCI 0.1% ophthalmic solutions is higher among patients with allergic conjunctivitis. So, it is recommended that every patient who present with allergic conjunctivitis may be managed with this drug. However, it is also required that every setup should have their surveillance in order to know the frequency of the efficacy of the drug.

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GLANZMANN'S THROMBESTHENIA; CLINICAL SPECTRUM AND DIAGNOSIS

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Abstract
Glanzmann's thrombasthenia (GT) is an inherited bleeding disorder resulting from either qualitative or quantitative abnormalities in the glycoprotein IIb/IIIa complex located on the platelet membrane. GT is marked by muco-cutaneous bleeding, normal platelet counts, and prolonged bleeding times.GT patients can be classified as type I, with less than 5% GPIIb/IIIa and absent clot retraction; or type II with 10-20% GPIIb/IIIa and minimal clot retraction. Diagnosis of GT is based on absent aggregation in response to ADP, collagen, epinephrine, thrombin and arachidonic acid and with a normal response to ristocetin, as well as flow cytometry studies of GPIIb-IIIa receptors using monoclonal antibodies.
Aim: The aim was to study the diverse clinical manifestations and approach towards diagnosing Glanzmann's thrombesthenia
Methods: It was a retrospective, descriptive study carried out in Department of Hematology, Children Hospital and Institute of Child Health Lahore for duration of two years.
Results: Out of total 250 patients 105(62.5%) were diagnosed with Glanzmann's thrombesthenia. Median age of diagnosis was 6.5 years and male to female ratio was equal. Commonest clinical manifestations were bruising and mucosal bleeding. Almost all the patients had normal platelet count and majority had raised bleeding time. On platelet aggregometry total absent response to ADP, collagen and epinephrine and normal response to ristocetin was found.
Conclusion: GT has leading frequency among other platelet function because of increased severity. Type1 is more common with normal platelet counts raised bleeding times and absent response to aggregating agents except ristocetin.

Glanzmann thrombasthenia is a rare disease, occurring at a frequency of approximately 1:1,000,000, however it is more prevalent in certain ethnicities. It is an autosomal recessive bleeding syndrome affecting the megakaryocyte lineage, molecular basis of which is linked to abnormalities of α IIbβ3 integrin.[1] Clinical manifestations of this disorder results from either qualitative or quantitative abnormalities in the glycoprotein IIb/IIIa complex located on the platelet membrane resulting in faulty platelet aggregation and diminished clot retracation.[2] The symptoms may vary in frequency and intensity in different patients. Recurrent epistaxis, gingival bleeding and menorrhagia are common symptoms while gastrointestinal bleeding, intracranial hemorrhage and hematuria have a lower incidence.[3] There is an increased risk of bleeding after surgical and dental procedures and increased bleeding poses a major problem after accidents and trauma.[4]

GT is marked by muco-cutaneous bleeding, normal platelet counts and morphology, and prolonged bleeding times. GT patients can be classified as type I, with mutation in ITGA2B gene, less than 5% GPIIb/IIIareceptors and absent clot retraction; or type II with mutation in ITGB3, 10-20% GPIIb/IIIa receptors and minimal clot retraction[5]. However , in variant form of GT there is a functional defect of the integrin αIIbβ3 complex.[6] The diagnosis of inherited platelet disorders require extensive laboratory investigation, as routine laboratory tests are not sufficient for differential diagnosis, and most of the specific tests are not readily available in many countries.[7] Diagnosis of GT is based on absent aggregation in response to ADP, collagen, epinephrine, thrombin and arachidonic acid and with a normal response to ristocetin in platelet aggregation studies , as well as flow cytometry and western blot studies of

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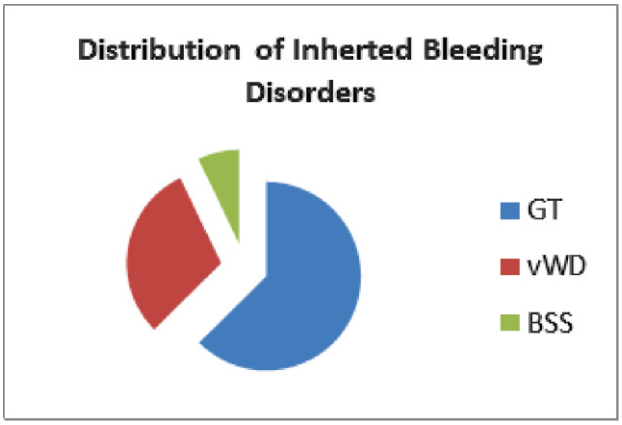
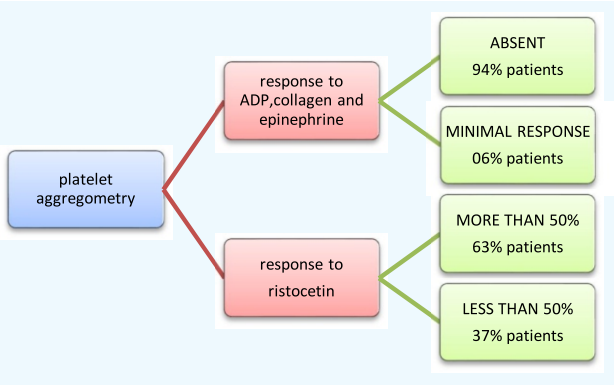


Age	<1 year	1-5 year	5-10 years	10-15 years	>15 years
%age	14%	38%	20%	20%	05%

Brusining (spontaneous and induced)	87%
Gum bleeding	83%
Nose bleeding	75%
Prolonged bleeding after trauma	30%
Malena	16%
Hematuria	05%
Eye/ear bleeding	01%

GPIIb-IIIa receptors using monoclonal antibodies.[8]



OBJECTIVE

The aim was to study the diverse clinical manifestations of GT patients and diagnostic approach towards establishing a final diagnosis Glanzmann's thrombesthenia.

METHODOLOGY

It was a retrospective, descriptive study carried out in Department of Hematology and Transfusion Medicine, Children Hospital and Institute of Child Health Lahore for duration of two years from June 2013- May 2015. All patients irrespective of age and gender presenting with bleeding symptoms and having normal platelet count were evaluated. Demographic details, relevant clinical history along with results of complete blood count, bleeding time and platelet aggregation studies were retrieved through data base and evaluated for the diagnosis of Glanzmann's thrombasthenia.

RESULTS

Total 250 patients presenting with variable bleeding symptoms were studied, out of which 168(67%)were diagnosed with various forms of rare inherited bleeding disorders. Glanzmann thrombesthenia comprised the major chunk of the patients, approximately 62.5% (105 patients) of total study group. 30.3% (51 patients) were diagnosed with von willibrand disease and 7.1% (12 patients) were found to have Bernaud Soulier syndrome. There was an equal gender distribution of disease. Median age of diagnosis of 6.5 years with majority of patients falling in 1-5 years age bracket. Patients were equally distributed between urban and rural populations. There was a vast spectrum of clinical manifestations ranging from bruising and nose/gum bleeding to eye/ear bleeding. Patients received all sorts of blood products for control of bleeding including FFPs, platelets and PCVs, but none of them received recombinant factor VII. Mean platelet count was 411.Only 5% patients had platelet count less than 100. Bleeding time was raised in 80% of the patients and normal in the remaining group. On platelet aggregometry, there was total absent response with ADP, collagen, epinephrine in 94% of cases and 06% had minimal response. 63% cases had more than 50% response with ristocetin while 37% had less than 50% response.

DISCUSSION

GT is an autosomal recessive inherited bleeding with increase frequency in certain racial groups, those in which consanguinity is common. Consanguineous marriages are common occurrence in Pakistani population, increasing the frequency of otherwise rare bleeding disorder. The Pakistan Demographic and Health Survey revealed that two thirds of unions in Pakistan are consanguineous[9]. In our study, almost all of the cases were born to consanguineous parents.

There was no gender discrimination in the group and cases were equally distributed in both male and female gender, although majority of late presenting cases were females coming with the symptoms of menorrhagia. The patient were uniformly presenting from both the big cities and

peripheral areas of the country. Most of the patients presented in first decade of life, and almost half of the cases were aged between 1-5 years of age. Median age of diagnosis was 6.5years. Because of the increase severity of symptoms the patients presented early in life. The symptoms had a wide spectrum ranging from bruising (spontaneous and induced) in 87%,nose bleeds in 83% gum bleeds in 75%, prolonged bleeding after trauma in 30%, malena/ hematochezia in 16%, hematuria in 05% and eye/ear bleed in 01% of patients. The ISTH-BAT score was significantly higher in those diagnosed with bleeding disorder as compared to normal people (33%) in the study group. Similar findings were found out by Lowe et al in a study published in 2013, that ISTH-BAT score in participants with suspected inherited platelet function disorders (interquartile range [IQR] 8-16) was significantly higher than in healthy volunteers (IQR 0-0).[10] Patients presented from variable backgrounds and referred from different setups, they received all sorts of treatment to control their bleeding episodes, almost 70% of the patients had antifribinolytic therapy atleast once during their course of disease and 25% received packed cell transfusions, 22% received FFPs and 25% received platelet transfusions. None of the patients received recombinant factor VII for their bleeding symptoms, mainly because of the high cost of the product and non-affordability of general public. Borhany at el reported that if bleeding did not responded to local pressure and antifibrinolytics, platelets and rVIIa was the next choice for the patients.[11] On investigations, most of the GT patients have normal platelet count. The mean platelet count was 411, well within the normal range. Bleeding time was prolonged more than 9 minutes in 80% of the patients, but 20% patients had normal bleeding times. Caen at el reported fifteen cases of Glanzmann thrombesthenia with normal platelet count and bleeding time.[12] On platelet aggregometry , response of platelets was checked as ADP, epinephrine, collagen and ristocetin. Almost all of our patients did not respond to ADP, epinephrine and collagen and more than 50% response with ristocetin. ISTH guidelines suggests to tests LTA responses to epinephrine, ADP, collagen, arachidonic acid (AA) and ristocetin should be assessed.[13]

CONCLUSION

GT has leading frequency among other rare bleeding disorders because of increased severity. There is an equal distribution among male and female population. Most common presentation is between age 1 to 5 years. Bruising is the commonest presenting complaint. Patients were transfused with all types of blood components. Platelet counts a,e normal in nearly all patients. Bleeding time was raised in majority of patients. Type 1 is more common as there is total absent response with agents other than ristocetin.

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FREQUENCY OF CHRONIC DIARRHEA AMONG PATIENTS WITH HUMAN IMMUNODEFICIENCY VIRUS INFECTION IN DERA GHAZI KHAN

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Abstract

Diarrhea is one of the most common GI symptoms in HIV patients. Diarrhea has many possible reasons and is an early sign often in acute HIV infection.

Objective: To assess the frequency of chronic diarrhea among patients with human immunodeficiency virus infection (HIV) presenting in teaching hospital of Dera Ghazi Khan.

Methods: A cross-sectional study was carried out at the department of Internal Medicine, Teaching Hospital of D.G Khan from November 29, 2015 to April 28, 2016. Subjects who fulfilled the inclusion criteria were enrolled in the study by non-probability, consecutive sampling technique. Consent was taken from all the patients. Data was collected on a pretested questionnaire, entered as well as analyzed by Statistical package of social sciences (SPSS) version 20.0. To see comparisons between genders, age groups, duration of HIV and diarrhea, chi square test was applied. For statistical significance P value was considered and <0.05 was the cut off value.

Results: In our study mean age of the patients was 28.59±6.66 years, the male cases were 183(63.10%) and the female cases were 107(36.90%). Diarrhea was present in 143(49.31%) HIV patients. Statistically significant difference was found among male & female HIV patients for having diarrhea (p=0.000).

Conclusion: Frequency of chronic diarrhea was 49.31% among patients with human immunodeficiency virus infection (HIV) presenting in teaching hospital, DG Khan. Male gender was more prone to have diarrhea than females.

Keywords: Chronic Diarrhea. Human immunodeficiency virus. HIV infection.

Acquired Immune Deficiency Syndrome (AIDS)/ Human Immunodeficiency Virus (HIV) have been known as major health, social and economic issue since last three decades. Infection has been spread globally with highest prevalence in Africa. Although a lot of work has been done on this deadly disease till date but still efforts are required for further improvement in prevention and management while dealing with infection and its complications.[1,2]

Pakistan is facing great threat of AIDS/HIV infection in different regions of the country. However currently the frequency is not very high but the sum of the new cases has been constantly increasing over the period of time. Sum of the registered cases reached as high as 6000 in the year 2010 and the number is constantly increasing along with the time involving individuals of all ages. For preventing this deadly disease, several thoughtful policies must be executed timely.[3]

Regardless of the availability of extremely active antiretroviral therapies (HAART), diarrhea is still a significant complaint for AIDS/HIV patients and had adversely affected patient's quality of life leading to cessation or substitution of HAART treat-

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ment. Opportunistic infections leading to diarrhea are considered rare since the availability of HAART. So the remaining causes are either noninfectious including treatment related adverse effects or enteropathy due to HIV.[4] Diarrhea significantly affected social life of 40 % of patients infected with HIV in a survey.[5]

In a study conducted in India, chronic diarrhea was present in 60.39% cases of HIV infection.[6] But in another study, it has been stated that chronic diarrhea was present only in 25.2% cases of HIV infection.[7] Whereas prevalence was reported 30.6% before treatment, 25.6% in early and 14.3% in late treatment phases in another study.[8] Sixty two percent subjects gave history of chronic diarrhea among 50 patients.[9]

While finding the reason of diarrhea Velasquez JN etal. enrolled 143 patients having HIV and chronic diarrhea, among them 12.6% had an opportunistic infection Microsporidiosis.[10] Warren S etal. found middle aged Caucasian positive for HIV infection, he had chronic diarrhea since 8 years and even after starting treatment the diarrhea could not settle. On further exploring the cause intestinal spirochaetosis was found to be the reason for diarrhea.[11] In a comparative study of 248 patients, prevalence of intestinal parasites was 82.3 % in treatment group and 84.6 % in pre-treatment group. The difference was not statistically significant and low CD4 count was associated with diarrhea.[12]

The number of HIV patients was increasing in DG Khan. Most of them presented with chronic diarrhea. Literature reported that HIV may be associated with high risk of chronic diarrhea due to immunodeficiency but controversial evidence has also been noted in literature as mentioned earlier. There was no local evidence of the frequency of chronic diarrhea in local population (DG KHAN) with HIV sero-positivity. As frequency of diarrhea was not established among HIV/AIDS patients & Frequency as baseline data is the first step for any planning, by knowing the frequency proper targets can be set to achieve a better response that includes timely management & prevention in future by further studies. So the objective of current study is to find the frequency of chronic diarrhea among patients infected with HIV presenting in teaching hospital, DG Khan.

METHODOLOGY

A cross sectional study was carried out at the department of Internal Medicine, Teaching Hospital of D.G Khan from November 29, 2015 to April 28, 2016. Calculated Sample size was 290 at 95% confidence interval and 5% margin of error with expected frequency of chronic diarrhea 25.2% among HIV positive patients.[7] Where HIV infection was considered when patients found positive for HIV by ELISA. Passage of watery or loose stools with a frequency of three or more in a day lasting for over 4 weeks was labeled as chronic diarrhea.

Patients of age range 18-40 years of either gender found positive for HIV were counted in the research through non probability consecutive sampling. All the study subjects gave permission for participation. Patients receiving any specific anti-diarrheal therapy in the previous two weeks were excluded from the study.

Data was collected through a pre tested questionnaire containing questions regarding demographics of patients (name, age, gender) & history. Patients were asked for history and duration of diarrhea. If the frequency of motion >3/day, consistency is low and duration of condition is >4weeks, then chronic diarrhea was labeled (as per operational definition).

Data was collected on a pretested questionnaire, entered as well as analyzed by Statistical package of social sciences (SPSS) version 20.0. Mean and standard deviation were measured for age, duration of HIV infection and diarrhea. Frequency and percentage was measured for gender and chronic diarrhea. To see comparisons between genders, age groups, duration of HIV and diarrhea, chi square test was applied. For statistical significance P value was

considered and <0.05 was the cut off value.

RESULTS

Study was conducted on 290 subjects, 28.59± 6.66 year was the subjects mean age where 18 & 40 years were minimum and maximum ages respectively, among them 183(63.10%) subjects were male and 107(36.90%) were female.

Mean value of HIV duration of the study subjects was 2.95±1.43 months with minimum one month and maximum five months duration.

The study results showed that the diarrhea was present in 143(49.31%) HIV patients and it was absent in 147(50.69%) HIV patients.

Mean value of the diarrhea duration of the study subjects was 2.13±2.48 weeks with minimum 0 weeks and maximum 6 weeks duration.

In this study 43(14.8%) patients appeared with 2-4 weeks duration of diarrhea, 14(4.8%) patients appeared with less than 2 weeks duration, 86(29.7%) patients appeared with more than 4 weeks duration of diarrhea and 147(50.7%) patients appeared with no diarrhea.

Statistically insignificant difference was found between age groups of the patients (Table 1).

Statistically significant difference was found for the presence of diarrhea among male & female gender (Table 2).

Statistically insignificant difference was found between the duration of HIV & diarrhea (Table 3).

Table 1: Age & Diarrhea

		Diarrhea		Total	Chi square (p-value)
		Present	Absent		
Age in years	≤30	78	90	168	1.32 (0.249)
	>30	65	57	122	
Total		143	147	290	

Table 2: Gender & Diarrhea

		Diarrhea		Total	Chi square (p-value)
		Present	Absent		
Gender	Male	105	78	183	12.91 (0.000)
	Female	38	69	107	
Total		143	147	290	

Table 3: HIV Duration & Diarrhea

		Diarrhea		Total	Chi square (p-value)
		Present	Absent		
HIV duration (months)	<3	87	92	179	0.094 (0.760)
	>3	56	55	111	
Total		143	147	290	

DISCUSSION

Number of registered cases of AIDS / HIV in Pakistan has been steadily increasing since 1987. Total number of reported patients reached 6,000 by 2010, a figure that has increased many folds over time.[3]

Chronic diarrhea is the commonest concern for patients infected with HIV, especially those with advanced disease. Diarrhea is a frequently presented complication among HIV patients and has significant medical implications. Although historically infection was the foremost source of diarrhea in HIV patients, later with the extensive practice of antiretroviral therapy, non-infectious diarrhea has arisen asa significant problem of HIV/AIDS population.[13]

In our study, 290 HIV patients were registered. The prevalence of chronic diarrhea in HIV cases was 49.31% (143 cases). No diarrhea was reported in 147(50.69%) HIV patients. Mean value of the diarrhea duration of the study subjects was 2.13± 2.48 weeks with minimum 0 weeks and maximum 6 weeks duration. Forty three (14.8%) patients appeared with 2-4 weeks duration of diarrhea, 14(4.8%) patients appeared with less than 2 weeks duration, 86(29.7%) patients appeared with more than 4 weeks duration of diarrhea and 147(50.7%) patients appeared with no diarrhea.

Some studies support the results of our study. In a study conducted in India, chronic diarrhea was present in 60.39% cases of HIV infection.[6] In another study Shankar U et al found all the HIV subjects enrolled had diarrhea. Among them 31 subjects (62%) had chronic diarrhea lasting for more than two weeks whereas rest of the 19 subjects (38%) had acute diarrhea.[9]

A further study by Mohammed et al. reported

that diarrhea was more prevalent in people with HIV (99 subjects, 51.1%) than in non-HIV patients (53 subjects, 29.5%). Irrespective of the state of diarrhea, frequency of gut parasites among patients with HIV was 44.8% and among uninfected HIV subjects was 34.4%. Among 192 patients with HIV, 28.1% had chronic diarrhea whereas 23.4% has acute diarrhea.[14]

Other studies show low prevalence when compared with current study's findings. In a study, it has been stated that chronic diarrhea was present only in 25.2% cases of HIV infection.[7] In a study conducted by Rubaihayo J and colleagues on 108,619 HIV positive patients, prevalence of infective diarrhea among HIV patients was 30.6% before HAART, 25.6% in early HAART and 14.3% in late HAART.[8]

A study was conducted to investigate the emotional impact of diarrhea on the life of HIV/AIDS patients. Out of 100 subjects interviewed 29 had diarrhea and confessed emotional distress. Their inability to control diarrhea, fear of fecal incontinence and dirty feeling in public were the main stress causing factors. To avoid such problems, they restricted their outdoor stay and avoided public gatherings.[5]

In an-other study conducted by Senya Chin et al, findings were quite different where Cryptosporidium infection was found present among both the study group (40%) with diarrhea and the control group (53%) without diarrhea.[15]

In current study statistically insignificant difference was found between age groups of the patients. There were two groups, one included 30yrs and below and other included all above 30yrs. In a study of 80 subjects 37 patients belonged to age group of 30-40 years and majority belonged to this group like our study.16In another study of demographic characteristics subjects belonged to ages from 18 to 90 years with mean age 36.4, only 12% of the subjects belonged to age above 50 years.[17]

In current study statistically significant difference was found for the presence of diarrhea among male & female gender. Male patients were more prone to develop diarrhea. Similar finding were reported by a study where gender distribution among HIV patients with diarrhea was like this, 75.9% males, 20.7% females, and 3.4% transgender.[5] another study reported different findings while considering gender, prevalence of diarrhea among females was consistently higher before and after treatment (p value < 0.05).[8] Where another study could not establish any association between gender and diarrhea.[17]

Statistically insignificant difference was found between the duration of HIV & diarrhea. This association was never studied and addressed before directly. A strong negative association was established in a study between the presence of diarrhea and CD4 count and subject with chronic diarrhea had lower CD4 cell counts. As the disease progress low immunity leads to low CD4 count and more infections.[9,16] None of the studies opposed this finding.

LIMITATIONS

Non-probability sampling & cross-sectional study design.

RECOMMENDATIONS

Early diagnosis, treatment, health education, patient and family awareness, prevention and management of diarrheal episodes are highly recommended among HIV patients. Additional studies are desired to investigate in detail for the reasons of diarrhea and prevention among HIV patients.

CONCLUSION

The prevalence of chronic diarrhea was 49.31% among patients with HIV infection in the teaching hospital, DG Khan. Male HIV patients are more likely to have diarrhea than females.

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MIGRAINE, ADIPONECTIN AND SOCIOECONOMIC STATUS

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Abstract

Background: Migraine, a primary headache syndrome, pries 16% inhabitants globally. Raised serum adiponectin (ADP) levels are associated with migraine pathophysiology. Contemporary research link socioeconomic inequalities with migraine in various aspects. Different mediators are under ongoing research for the association of socioeconomic status (SES) with migraine. Serum ADP levels can bring about the missing piece of this association. Identifying the relation of SES with migraine will help us better understand disease course.

Objectives: The objective of this study was to compare serum adiponectin levels in migraine patients and controls stratified on the basis of SES.

Design: It was a cross sectional study.

Place and duration of study: It was conducted in Shaikh Zayed Hospital, Lahore, in 6months, September 2015 – February 2016.

Methods: Serum ADP levels were measured and compared in 80 migraineurs and controls stratified in low, middle and high SES groups.

Results: In high SES group 66.7% migraineurs had high ADP levels while 7.1% of controls had high ADP level. The difference is significant ($P \leq 0.05$).In middle and High SES groups the difference was insignificant. Odds Ratio (OR) in low and middle SES group showed that high adiponectin level is risk factor for migraine especially in low SES group. Though, in high SES group contrary results obtained, OR showed that it is not a risk factor in this group.

Conclusion: High ADP levels are statistically significant in low SES migraine population. Elevated serum ADP levels are risk factor for migraine in middle and low SES individuals.

Key words: Adiponectin, migraine, socioeconomic status.

Migraine is debilitating and ubiquities primary headache syndrome affecting 16% of population across the globe.[1,2] Mundane and devastated social, mental and physical well-being of patients is hallmark of disease course. The climax of disease prevalence strikes at the age range of 25-55 years, the most prolific and dynamic span of one's life.[3] Lagging behind in educational accomplishments, appalling student related assignments, and tedious family relationships have been reported in number of migraine sufferers that may bring about colossal personal and societal burden. Deficient and abysmal workplace performances cause dire economic consequences and repercussions which steer towards instability in occupational achievements.[4,5]

World Health Organization (WHO) consigned this distressful headache syndrome with the other debilitating health conditions like dementia, quadriplegia and psychosis.[6] Migraine is defined by "international headache classification" as "recurrent incapacitating neurovascular disorder with episodes of about 4 to 72 hours duration of unilateral, pulsating, and moderate to severe debilitating pain that is aggravated by movements and is associated with photophobia, phonophobia, nausea and vomiting".[7]

ADP, produced by subcutaneous and visceral adipose tissues, is predominantly involved in sundry energy homeostasis, certain metabolisms of fats, carbohydrates and proteins and various inflammatory processes. Gene of ADP is on Chromosome

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3q27 and it is composed of 244 amino acids.[8,9] Though a number of receptors of ADP have been discovered which are expressed in different organs but adipo R1 (adiponectin receptor 1) and Adipo R2 (adiponectin receptor 2) are abundant in brain, especially in brainstem.[10]

Pathophysiology of migraine, though cryptic, but is largely attributed to trigeminovascular system activation accompanied by raised serum ADP levels.[11,12] Proinflammatory nuclear factor kappa β (NF-κβ) pathways, which are activated in acute attacks of migraine, are stimulated by ADP. Besides, release of proinflammatory cytokines, IL-6, TNF-αand nitric oxide is also triggered by raised levels of ADP.[13,14]

Vessels of brain are innervated by trigeminovascular system. The trigeminovascular system supplies to the periaqueductal grey area, locus coeruleus, hypothalamus and some parts of thalamus. These ascending connections are carried out by trigeminothalamic and trigeminohypothalamic projections. Nociception during acute attack of migraine and inflammatory changes are caused by vasoactive intestinal peptide, CGRP (calcitonin gene regulated peptide), substance P and nitrous oxide.[15,16,17]

A number of health conditions have been studied in relation to socioeconomic strata. The idea is to deduce potential targets for prevention and minimizing deleterious effects of disease on health outcome. Dissimilarity of socioeconomic status as devised by occupation and income gives divergence to health status of disease sufferers.[18] Drawing a connection between socioeconomic status and an illness with as huge prevalence as migraine is of utmost significance and importance from public health outlook. Contemporary institutes toiling at surveying the impact of socioeconomic status on migraine. Higher incidence of migraine in lower socioeconomic status groups is compatible with the social causation hypothesis.[19] Low socioeconomic status is associated with an increased prevalence of migraine. Documentation of increased attacks of migraine in population of low socioeconomic status has been evinced. Hitherto, the pathophysiology of different underlying mechanisms which may find a connection of disease to socioeconomic status are still vague and elusive.[20]

The objective of this study was to compare serum adiponectin levels in migraine patients and controls stratified on basis of socioeconomic status i.e. low socioeconomic status, middle socioeconomic status and high socioeconomic status. Variance in results of serum adiponectin levels in different socioeconomic strata can help to find the association of ADP levels with respective group of population.

Correlation and relevance of serum ADP levels and socioeconomic status in migraine sufferers can succor ministration in devising more desirable treatment plans, improved comprehension of disease course and ameliorated prophylaxis. Like some of the pertinent studies, this topic still yearns for cogitation as diminutive data is available to be conclusive.

METHODOLOGY

Our study was a cross sectional, comparative study conducted at Federal post-graduate medical institute Shaikh Khalifa Bin Zayed Al-Nahyan, Lahore, and clinical out-patient department of neurologyat Shaikh Khalifa Bin Zayed Al-Nahyan, hospital, Lahore, after taking permission from the respective head of departments. The time span of our study was six months.

A study population comprising 80 individuals was selected consisting of controls and migraine patients. 40 Controls were recruited. They were healthy personages without signs, symptoms or complaints of migraine. They were selected from MBBS students and faculty and staff of Federal post-graduate medical institute Shaikh Zayed, Lahore. 40 migraine patients were included in our research project. They were diagnosed clinically by neurology consultants.

Convenient (non-probability) sampling was done.

The Inclusion Criteria:

Male and female migraine patients with

- Age range of 18-40 years
- BMI range of 18.5-24.9 kg/m2

The Exclusion Criteria:

Healthy individuals and migraine sufferers presenting with headache due to causes other than migraine i.e. other primary headache syndromes e.g. tension headache and cluster headache. The socioeconomic groups were defined based on their occupation and household income. They were divided into three groups i.e. low socioeconomic status group, middle socioeconomic status group and high socioeconomic status group.

After getting informed consent in written, provided to participants, the complete demographic data of all the individuals was convened. Assessment and evaluation of the subjects was carried out by taking explicit history and a comprehensive, especially delineated questionnaire. Blood samples were drawn from patients under complete hygienic conditions. Serum Adiponectin levels were estimated by using ELISA technique in laboratory of Pathology department of Shaikh Zayed Hospital, Lahore.

The data was entered into and analyzed by SPSS (Statistical Package for Social Sciences) version 20.0. Data was stratified for socioeconomic status of patients. Mean ADP levels were compared in groups by using independent sample t-test for all strata. Similarly, raised ADP levels were compared in groups by using chi-square test for each stratum. Odds ratio was found to measure association. P-value≤0.05 was considered significant.

RESULTS

DISCUSSION

In this research three socioeconomic strata were made i.e. low, middle and high socioeconomic status groups, devised on basis of occupation and household incomes. In each stratum serum ADP levels were measured and analyzed in age and BMI matched comparative groups which included migraineurs who fulfilled the criteria of diagnosis for migraine, and a healthy control group. Mean age of control group was 30.10±7.02 years and that of migraine group was 28.7±6.8 years. While BMI of control groupand that of migraine group was 21.43±2.02kg/m^2 and 22.08±1.94kg/m^2 respectively.

Data was stratified for socioeconomic status of patients. In low socioeconomic status group patients, 10(66.7%) patients of migraine had raised ADP level while in controls only 1 (7.1%) subject showed high ADP level. The difference was significant (P< 0.05). In middle socioeconomic status stratum, 7 (58.3%) patients of migraine evinced elevated ADP level while in controls, 5 (45.5%) individuals had high ADP level. The difference was insignificant (P> 0.05) in middle socioeconomic stratum. In high socioeconomic stratum, 5 (38.5%) patients of migraine manifested high ADP level while in controls, 6 (40.0%) participants exhibited elevated ADP level. The difference was insignificant (P>0.05).Odds ratio (OR) in both low and middle socioeconomic groups showed that it is a risk factor for migraine, especially for patients of low SES (26.000 & 1.680 for low and middle SES, respectively). But in high SES group, the OR showed that high ADP may not be a risk factor for migraine (OR=0.938). Our findings are in line with the research conducted by Bigal et al. They laid bare the low socioeconomic status effectuates upsurge prevalence of migraine even though unescorted biological predisposition. Low socioeconomic status also directs increased incidence of migraine and protracted duration of illness.[21] Anke et al. also manifested pervasiveness of migraine in association with the low socioeconomic status, they also found elevated odds ratio for migraine attacks.[20] Charelston et al concluded in his research work that progression of disease and worst outcome of disease characters were characteristics of the underinsured and uninsured population as this group of population had to face difficulty to approach to neurology specialists and financial limitations to proper medical care.[22] Another study overviewed the subject matter and formulated the execrable disease presentation in underserved population.[23]

Certain limitations should be contemplated while transcribing our findings. The information regarding socioeconomic status variables are self-reportedso prospective under reporting and miscalculations are conceivable. Meticulous and fastidious studies should be entailed with carefully constructed design and methodology to assiduously study infor-

Table 1:

SES	ADP level	Group		Total	p-value	OR
		Migraine	Control			95% CI
Low	High	10 (66.7%)	1(7.1%)	11 (37.9%)	0.001*	26.000
	Normal	5 (33.3%)	13(92.9%)	18 (62.1%)		2.607-259.295
	Total	15 (100.0%)	14(100.0%)	29 (100.0%)		
Middle	High	7 (58.3%)	5 (45.5%)	12 (52.2%)	0.537	1.680
	Normal	5 (41.7%)	6(54.5%)	11 (47.8%)		0.322-8.756
	Total	12 (100.0%)	11(100.0%)	23 (100.0%)		
High	High	5 (38.5%)	6(40.0%)	11 (39.3%)	0.934	0.938
	Normal	8 (61.5%)	9(60.0%)	17 (60.7%)		0.205-4.294
	Total	13 (100.0%)	15(100.0%)	28 (100.0%)		

mation on migraine features and frequency to avoid warped and under reported history by patients. Above stated limitations are needed to be considered in the forthcoming studies.

CONCLUSION

Albeit, contemporaneous research is streaming, no study is published in Asian population regarding this subject. This workpiece would aid in studying imminent concept of relation of migraine and socioeconomic status by tying in pertinent serum adiponectin levels. Our study will not only orchestrate better cognizance of disease course, but also it would be propitious in devising prevention strategies and revamped treatment models.

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INFLUENCE OF GENDER AND OTHER FACTORS ON SPECIALTY PREFERENCE OF DOCTORS IN PUNJAB, PAKISTAN

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Abstract

Objective: To determine the specialty preferences of male and female doctors in Punjab province and to study the factors associated with these preferences.

Methods: Questionnaire-based data was collected from 385 medical doctors with equal gender ratio, in various clinical specialties after informed consent. All were based in Punjab and registered with Pakistan Medical and Dental Council and University of Health Sciences by the year 2012-2013. Results were evaluated by Chi Square test to compare the gender difference in choice of specialty and the influencing factors.

Results: Significantly more female doctors were found to choose radiology and obstetrics & gynaecology and more males opted for medicine, surgery and ENT in sample population. Among the personal factors, "a better income expectation" was most influencing factor for males and"Work-life balance and "No night calls" for female doctors. Role models and professional independence were most important professional factors for males and females respectively.

Conclusion: Factors in career choice are complex and vary by gender and specialty. This study elucidated not only the gender differences in specialty preference but also the factors associated with them. These differences can influence the current and future maldistribution of specialties. Systematic changes in working environment of medical profession are required to solve this problem.

Keywords: Medical graduate, medical practitioners, medical specialties, career choice, gender

Probing the gender differences in medical specialties choice has become imperative as the student population in medical colleges is changing throughout the globe towards a majority of female students, which has raised concerns about medical professionals' career advancement in gender terms.[1-2] Among most important reasons of this disquiet is are; to what extent young male and female medical professionals i.e. house officers and residents make similar or different specialty choices and how will it fit the demands of various medical specialties and community needs.[3]

Earlier studies on this topic have shown that the choice of specialty is related strongly to gender. In most instances, male students choose for technical and instrumental oriented specialties and female students are more relationship oriented.[4-5] Phil Heiligers has classified the reasons behind these differences into three perspectives viz., gender, stage of life and motivational perspectives and he pointed out that despite females are more than males in medical schools in Netherlands, they are very few who keep working till the level of becoming consultants except for gynaecology and paediatrics which are traditio-

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nally associated with the gender role of women.[3] Secondly, transitions between the stages of life, such as marriage or becoming a parent, have an impact on social roles, relationships and choices for the future.[6] Medical students have to spend long period of time in their studies and training before they start a career as a specialist. Such transitions in the last years of their life as a student influence quite strongly on their choice of a specialty, because ideas of a partner or responsibilities towards family life, can direct the specialty choice. Furthermore, these students are confronted with conflicting roles. Being a student and partner can limit their preferences towards less challenging specialties[7]. Thirdly, males and females also differ in their motives for their specialty choice.[8] Generally, male students are more motivated by salary, status and the opportunity to implement technical activities whereas female candidates are motivated by humanist and altruistic reasons.[9]

These issues demand to be addressed by medical educationists, policy makers and all other stakeholders in order to achieve a balanced distribution of doctors among all specialties however there is limited data available from Pakistan.[10] Thus, we performed current study to explore the actual state of affairs regarding differences of specialty choice among male and female medical professionals working as specialists and consultants.

METHODology

Study Design and Participants

This observational study was conducted in August 2013 in Punjab, Pakistan. A total of 385 medical graduates were included in this survey after taking written consent. The participants were recruited from different demographic regions of Punjab i.e. Northern area 91(23.6%), Central 263(68.3%) and Southern 31(8.1%) according to the population density of medical professionals in the relevant regions of the province. The study protocol and data collection instrument were approved by ethical committee of University of Health Sciences, Lahore, Punjab.

Data Collection

Data about demographic profile (age, gender) and specialty choice was collected on a specially designed self-administered questionnaire which was distributed among the participants located in various cities of Punjab province. Factors influencing the choice of specialty were grouped into personal and professional factors/reasons and these factors were assessed through multiple questions shown in the same questionnaire.

Statistical Analysis

The data was analyzed using S.P.S.S. version 20.0 (Statistical Package for Social Sciences). Frequencies and percentages were given for qualitative variables (gender, specialty of choice). Chi Square test was applied to determine the association of choice of specialty with gender and the factors influencing the specialty selection. A p-value of ≤ 0.05 was considered statistically significant.

RESULTS

The study included 385 doctors working in various specialties with a mean age of 37±8 years out of which 192 (49.9%) were males and 193 (50.1%) were females. Gender differences were found in the specialties of medicine, radiology, surgery, obstetrics and gynaecology and ENT. Significantly more males opted for medicine, surgery, and ENT. Significantly more females opted for radiology and obstetrics &gynaecology. In medicine, 62 (62.6%) were males and 37 (37.4%) were females; hence significantly more males chose the specialty; p = 0.003. In radiology, 6 (20%) were males and 24 (80%) were females; hence significantly more females chose the specialty; p= 0.001. In surgery, 54 (83.1%) were males and 11 (16.9%) were females; hence significantly more males chose the specialty; p = 0.000. In obstetrics and gynaecology, all 40 (100%) were females; hence significantly more females chose the specialty; p= 0.000. In ENT, 8 (88.9%) were males and 1 (11.1%) were females; hence significantly more males chose the specialty; p= 0.018. No significant gender differences were

Table 1: Comparison of Gender difference Among Choice of different Specialties using Chi Square Test

		Frequency	Percent	P value*
Medicine	Male	62	62.6	0.003*
	Female	37	37.4	
	Total	99	100.0	
Basic sciences	Male	18	42.9	0.336
	Female	24	57.1	
	Total	42	100.0	
Anesthesia	Male	2	66.7	0.559
	Female	1	33.3	
	Total	3	100.0	
Radiology	Male	6	20.0	0.001*
	Female	24	80.0	
	Total	30	100.0	
Dentistry	Female	1	100.0	0.318
Surgery	Male	54	83.1	0.00*
	Female	11	16.9	
	Total	65	100.0	
Obstetrics & Gynecology	Female	48	100.0	0.00*
Paediatrics	Male	6	42.9	0.593
	Female	8	57.1	
	Total	14	100.0	
Pathology	Male	17	48.6	0.872
	Female	18	51.4	
	Total	35	100.0	
Ophthalmology	Male	8	50.0	0.992
	Female	8	50.0	
	Total	16	100.0	
ENT	Male	8	88.9	0.018*
	Female	1	11.1	
	Total	9	100.0	
Dermatology	Male	3	33.3	0.315
	Female	6	66.7	
	Total	9	100.0	
Psychiatry	Male	8	57.1	0.579
	Female	6	42.9	
	Total	14	100.0	

Statistically significant difference i.e. $p < 0.05$
Calculated using Chi square test

found in the specialties of basic sciences, anaesthesia, dentistry, paediatrics, pathology, ophthalmology, dermatology and psychiatry as shown in Table 1.

Gender Differences in Personal Factors

The personal factors where the male and female doctor's opinion differed included;

"Better income expectations" was reported by 81 (42.2%) male doctors and 59 (30.6%) female doctors whereas "Personal attitude towards life" was reported by 91 (47.4%) male doctors and 65 (33.7%) female doctors. "Work-life balance (less working hrs and ability to spend time with family)" was reported by 48 (25%) male doctors and 88 (45.6%) female doctors and "No night calls" was reported by 36 (18.8%) male doctors and 67 (34.7%) female doctors. Rests of the personal factors were not significantly different between male and female doctors as shown in Table 2.

Gender differences in Professional Factors

The professional factors where the male and female doctor's opinion differed included;

1. "My teacher of that specialty was a role model" was reported by 81 (42.2%) male doctors and 53 (27.5%) female doctors and "Professional Independence" was reported by 63 (32.8%) male doctors and 87 (45.1%) female doctors; this difference was statistically significant; p= 0.014 as shown in Table 3.

DISCUSSION

Gender differences in the choice of specialty have been reported by recent studies from US,[11] the Europe[12] and other parts of the world[9] and current study has shown that the similar exists in Pakistan too. However, what are those differences and how imperative they could be; is discussed here. We observed that these gender differences are mainly found in the choice of specialties of medicine, radiology, surgery, obstetrics and gynaecology and ENT. According to current study, significantly more

Table 2: *Comparison of Gender difference among Personal Factors for Choice of Current Specialty using Chi Square Test*

	Personal factors	Total	Males (192)	Females (193)	P value*
1	Personal interest 0.334	296	150 (78.1%)	146(75.6%)	0.564
2	Better income expectations 5.614	140	81 (42.2%)	59(30.6%)	0.018*
3	Some near one had some illness that was related to my choice of specialty 0.119	46	24 (12.5%)	22(11.4%)	0.739
4	Parental preference 1.867	77	34(17.7%)	43(22.3%)	0.262
5	Length of residency training during postgraduation 0.1675	57	27(14.1%)	30(15.5%)	0.682
6	Personal attitude towards life 7.514	156	91(47.4%)	65(33.7%)	0.006*
7	Work-life balance (less working hrs and ability to spend time with family)17.87	136	48(25%)	88(45.6%)	0.000*
8	No night calls 12.52	103	36(18.8%)	67(34.7%)	0.000*
9	Better academic results in my choice of specialty during studies in college 2.352	80	46(24%)	34(17.6%)	0.125
10	Opportunity to contribute to society 0.935	185	97(50.5%)	88(45.6%)	0.334
11	Better one to one interaction with patient. 0.488	143	68(35.4%)	75(38.9%)	0.484

* Calculated using Chi square test * Statistically significant difference i.e. p <0.05

Table 3: *Comparison of Gender difference among Professional Factors for Choice of Current Specialty using Chi Square Test*

	Professional factors	Total	Males (192)	Females (193)	P value*
1	My teacher of that specialty was a role model. 9.198	134	81 (42.2%)	53 (27.5%)	0.002*
2	More options for fellowship available.0.0702	96	49 (25.5%)	47 (24.4%)	0.791
3	Professional Independence. 6.0855	150	63 (32.8%)	87 (45.1%)	0.014*
4	Advice from peers. 0.1457	97	50 (26%)	47 (24.4%)	0.703
5	Inspiration during clinical rotation. 0.0624	158	80 (41.7%)	78 (40.4%)	0.803
6	Publically appreciated field. 0.1609	124	60 (31.3%)	64 (33.2%)	0.688
7	Prestige in medical community. 0.0330	126	62 (32.3%)	64 (33.2%)	0.856
8	Research opportunities 0.0209	117	59 (30.7%)	58 (30.1%)	0.885
9	Intellectual challenge. 0.9612	151	80 (41.7%)	71 (36.8%)	0.327
10	Fewer specialists in country in this specialty. 0.7754	87	47 (24.5%)	40 (20.7%)	0.379
11	Scope of specialty internationally 0.0042	147	73 (38%)	74 (38.3%)	0.948
12	Career counseling in medical college 2.73	42	26 (13.5%)	16 (8.3%)	0.098

*Calculated using Chi square test * Statistically significant difference i.e. p < 0.05

males opted for medicine, surgery, and ENT whereas significantly more females opted for radiology and obstetrics &gynaecology. Our results are consistent with a local study conducted in 2010 on 4th year medical students in which majority of females selected obstetrics and gynaecology whereas for males, surgery was the most preferred specialty.[13] Gender has its due role in the selection of obstetrics and gynaecology as a specialty. However, the cultural and religious reasons can be held responsible for the decreased number of male students in obstetrics and gynaecology.[14]

Lefevre et al.[15] surveyed 1780 medical students in France and reported that gender significantly influenced the choice of specialty – 88% of future paediatricians, 82% of gynaecologists and 77% of general practitioners were women. No significant gender differences were found in other specialties like anaesthesia, dentistry, pathology, ophthalmology, dermatology and psychiatry. A study on the choice of specialty among a group of Brazilian medical students found that women predominated in

paediatrics as compared to men who were opting for surgery and orthopedics, with no predominance of either gender in the other specialties.[16]

A similar pattern was seen in medical students of New Zealand where females were more likely to be interested in obstetrics and gynaecology, paediatrics, geriatrics, public health or general Medicine, and lesser in surgery, anaesthesia, emergency medicine than their male counterparts.[4] Alers et al.[17] included a group of 214 female and 78 male medical students in a longitudinal study and found that after three years, the male students remained highly interested in surgery, but the female students increasingly preferred gynaecology.

Stengler and colleagues[18] studied medical professionals' preferences for their specialties and found that both female and male physicians prioritized general medicine and internal medicine whereas female physicians preferred paediatrics and gynaecology and males frequently chose surgery. They also observed that women view professional cooperation opportunities, framework conditions for their family, and job-related commitments as important factors in their decision to establish a practice; quality of life, financial and working conditions are more important to men. A Japanese research in 2010 reported that the preference rates for general surgery, orthopedics, neurosurgery, and emergency medicine were significantly higher in men than in women, while those of obstetrics & gynaecology, paediatrics, and dermatology were higher in women[5].

Mahmood et al.[19,20] studied specialty choice among medical students of Saudi origin and found that the most preferred specialty expressed by male students was surgery, followed by internal medicine and orthopedics, whereas female students liked surgery, followed by paediatrics and ophthalmology. Male students' emphasized factors like less competitive field, shortage of specialists, and diversity of patients whereas the prestige of specialty and teaching opportunities had a greater impact on female students. Moreover, increased likelihood for contemporary female medical graduates to enter obstetrics and gynaecology compared with either primary care or surgery is consistent with other recent studies regarding gender differences in specialty choice.[21,22]

Current study shows that among the personal and professional factors which played an important role behind the choice of specialty were "Personal interest" and "Inspiration during clinical training" respectively.In a recent local study by Rehman et al.[14]the highly considered factors (regarding specialties) chosen by 70% of the medical students were: applicable to respective personalities of the individuals, prestige and respect, international opportunities, and time commitment. Surgical-skills, job availability, financial rating, academic performance, and a role model were moderately influencing factors. Hospital environment, parents, general practice, peer-pressure and personal health were the least influential.

In our study, male and female doctor's opinion differed both in domain of personal and professional factors. Better income expectations and role models were found to be more important for male doctors whereas work life balance and no night calls influenced females to specialize in a particular field. Similar to our study, Zarkovic et al.[23] found physician role models to play an important role in the specialty decision-making process for medical students. Another study revealed that mentors who are assessed (by students) as high quality teachers have a greatest influence on student career choice by up to four-fold. When students assess a mentor as being a negative role model, a poor teacher or lacking discipline specific knowledge, they will turn away from that field. The positive influence of relationships between mentors and students on career choice is strongest where there is persistent mentorship, enduring care, and continuity of patient interactions.[24]

Differing from our study, a survey from Kuwait quoted that "Looking for a good treatment outcome for patients" and a "challenging specialty" were the most influencing incentives when selecting a future specialty by medical students.[25] Similarly Boyd et

al.[26] reported that lifestyle and length of residency were strong influences, while attributing less influence to mentors. But as this study was on doctors from emergency medicine specialty, perhaps students choosing a career in this field have distinctly different priorities.

A study in nine US medical schools showed that the decision to have a family was a more significant influence for women than men.[27] Similar to this, our study also showed that "Work-life balance" and "No night calls" were significantly more important for female doctors. Akhund et al.[28] published a study on medical graduates from Dow International Medical College, Karachi on 148 students. Surgical (31%) and Medical (23%) specialties were the two most frequently selected fields. Paediatrics was chosen by 18% of the students. Most preferred reasons for choosing a particular specialty were high income potential (37%), influence of a role model in the specialty (32%), inclination for specialty before medical school (30%) and others.

All the observations of current study cannot be generalized to the whole country as the study has its own quite a few limitations, as it was conducted in only one province, which may not represent the whole country. Secondly, the main bulk of participants came from major teaching institutions. Also cross-sectional surveys are commonly associated with selection bias. Although random sampling was done but refusal rate was high so it is clear that only those doctors were included in this study who were easily approachable which concludes that this study sample may not be representative. Moreover, the influencing factors were given in the close ended questions which might have overlooked some other unidentified factors. Recall bias can be another limitation of this study as it is possible that the participants could not answer the questions correctly regarding the influencing factors that led to the decision of present specialty. These limitations should be taken into consideration while applying the results of current study as well as during the planning of future similar researches.

CONCLUSION

Male doctors most commonly prefer medicine, surgery, and ENT whereas significantly female doctors most commonly prefer radiology and obstetrics & gynaecology in Punjab. Better job expectations and personal interests influenced most male doctors whereas better life-work balance and role models influenced most of their female counterparts.

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" The question isn't how to get cured, but how to live."

RELATIONSHIP OF NEUTROPHIL TO LYMPHOCYTE RATIO AT THE TIME OF ADMISSION TO ADVERSE CARDIAC EVENTS IN PATIENTS HOSPITALIZED WITH ACUTE CORONARY SYNDROME

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Abstract

Objective: The objective of this study is to assess the utility of admission neutrophil to lymphocyte ratio (NLR) in predicting adverse cardiac outcomes during hospitalization in patients with acute coronary syndrome.

Methods: This cross sectional study was conducted in cardiology and pathology departments of Gulab Devi Teaching Hospital for 6 months from August 2017 to January 2018. Total 133 patients admitted with acute coronary syndrome were enrolled in study to see the association between neutrophil to lymphocyte ratio and adverse cardiac outcomes. Data was analyzed using SPSS version 21. RESULTS: Out of total 133 patients, 42 patients had high neutrophil to lymphocyte (NLR >3.0) of which 39 patients showed complications while 3 patients had no complication; 49 patients had intermediate NLR (NLR 1.5 – 3.0) of which 40 patients showed complications, while 9 patients had no complication; 42 patients had low NLR (NLR < 1.5), of which 23 patients showed complications while 19 patients had no complication. Mean age of patients was 56.39% with maximum age of 85 years and minimum age 25 years, 93(69.29%) were female and 40 (30.08%) were male patients. Overall high rate of adverse outcome was observed in patients with high neutrophil to lymphocyte ratio.

Conclusion: Higher neutrophil to lymphocyte ratio is associated with increases incidence of adverse cardiac events in patients admitted with acute coronary syndrome.

Key words: Acute coronary syndrome, myocardial infarction, neutrophil to lymphocyte ratio, Outcomes/ complications

Coronary artery disease (CAD) is one of the major causes of significant morbidity and mortality resulting in over 7 million deaths annually.[1] Multiple risk factors have been identified which cause increase incidence of CAD.[2] Acute coronary syndrome (ACS) is a terminology used to describe signs and symptoms resulting from myocardial ischemia. ACS is sub-classified as unstable angina, non–ST-segment elevation myocardial infarction (NSTEMI) and ST-segment elevation myocardial infarction (STEMI) based on ECG changes and cardiac biomarker levels.[3] Pathologically acute coronary syndrome (ACS) is characterized by unstable atherosclerotic plaque in cardiac vessels.

Despite appropriate treatment some patients with ACS may develop complications like ongoing ischemia, heart failure, pulmonary edema, arrhythmias etc. Because inflammation is considered to plays a key role in initiation and progression of obstructing plaque in epicardial vessels causing reduced coronary blood flow and symptomatic coronary artery disease,[4] detection of markers of inflammation such as white blood cell (WBC) and its subtypes can be used to predict occurrence of adverse cardiovascular events in patients presenting with acute coronary syndrome.[5] Neutrophil to lym-

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phocyte ratio (NLR), an easily measureable value is a good white blood cell predictor of adverse cardiac outcomes in acute coronary syndrome patients. The neutrophil–lymphocyte ratio (NLR) gives an idea of active inflammatory process in the coronary vessels during the active phase of this syndrome.[6] A higher NLR in an indicator of increased inflammatory activity in vascular bed which in turn represent excessive atheromatous disease formation in epicardial vessels.[7] Association between higher NLR and greater adverse cardiac events has been seen in patients with ACS.[8]

Neutrophil / lymphocyte ratio is measured from routine blood count examination which is easily available in every health care facility. Higher NLR ratio can be used to pick those patients who are more likely to have severe CAD and need aggressive treatment to reduce adverse cardiac events.[9] The rationale to conduct this study at our centre was to investigate the utility of admission NLR in predicting adverse cardiac events in our local patients population presenting with acute coronary syndrome.

METHODOLOGY

Setting: The study was conducted in the Pathology and Cardiology departments of Gulab Devi Teaching Hospital.

Duration of Study**:** The study was six months duration from 01/08/2017 to 31/01/2018

Study Design: Cross sectional study

Sampling: Non probability purposive sampling

Sample Size: The study was performed on 133 cases.

Inclusion Criteria: Patients with acute coronary syndrome were included in study based on ECG and echocardiography.

Exclusion Criteria:

1) Patient with acute illness, infection and chronic co-morbidities that might result in early death.
2) Patients who have disease other than acute coronary syndrome.

One hundred and thirty three cases of acute coronary syndrome meeting inclusion criteria were included in the study on the basis of non-probability purposive sampling. Informed consent was taken from all patients. The clinical and pathological data including clinical history, risk factors, ECG changes, and echocardiographic changes, neutrophil to lymphocyte ratio, age and adverse outcomes were recorded on the proforma. Later on a master data sheet was developed and all the information weas entered on SPSS. SPSS version 21.0 was used for statistical analysis by using original data of the clinical trial

RESULTS

One hundred and thirty three consecutive patients were entered into study. Proforma were filled with the required data and was statistically analyzed. In this study male patients were 40 (30.08 %) and female were 93(69.92%). Out of 133 patients 84 (63.13%) patients had STEMI, 44(33.08%) patients had NSTEMI. and 5(3.76%) patients had unstable angina. Of 133 patients, 42 patients (31.58 %) had high neutrophil to lymphocyte ratio, 49 patients (36.84%) had intermediate neutrophil to lymphocyte ratio while 42 (31.58%) had low neutrophil to lymphocyte ratio. Out of total 133 patients 102 (76.69%) patients had some complication while 31 (23.30%) patients remained free of any complication.. In our study out of 133 patients, total 42 patients had high neutrophil to lymphocyte (NLR) in which 39 patients showed complications, while 3 patients had no complications. Of 133 patients, total 49 patients had intermediate NLR of which 40 patients showed complications, while 9 patients had no complications. Out of 133 patients, total 42 patients had low NLR, of which 23 patients showed complications while 19 had no complications (Table 1). In our study out of 133 patients total 27 (20.3%) patients had arrhythmias, 09 (6.7%) had ongoing ischemia, 55 (41.3%) patients had left ventricular failure, 21(15.7%) patients had cardiogenic shock and 06 (4.5%) patients had heart failure. (Table2). In patients with a high NLR an increased incidence of arrhythmias, cardiogenic shock, pulmonary edema and thrombo-embolism was observed.

As the p value (p=0.000) is lesser than 0.05, it

indicates that there is significant association between neutrophil to lymphocyte ratio and adverse cardiac events in patient admitted to hospital with acute coronary syndrome.

DISCUSSION

Coronary artery disease clinically manifesting as acute coronary syndrome is an atherosclerotic process and inflammation plays an important role in atherogenesis. Neutrophil to lymphocyte ratio in blood gives an idea of systemic inflammation and its assessment can help to detect patients having greater risk of adverse cardiac events due to aggressive coronary artery disease.[14] We conducted a study of 133 cases to assess the association between admission neutrophil to lymphocyte ratio and in-hospital adverse cardiac events in patients admitted with acute coronary syndrome. Our study showed that high NLR was strongly associated with adverse cardiovascular outcomes including arrhythmias 22(52.38%), left ventricular failure 19(45.2%), cardiogenic shock18 (42.85%), pulmonary edema 6(14.2%), ongoing ischemia 2 (4.76%) and thromboembolism 4 (9.5%). A very interesting feature was that left ventricular failure and ongoing ischemia were more common in patients with intermediate NLR occurring as 28(57.14%) and 19(45.2%) respectively as compared to patients with high NLR 7 (14.28%) and 2 (4.76%). Neutrophils are believed to accelerate atherosclerosis by secreting inflammatory mediators while lymphocytes reduce atherosclerosis by regulatory T cells.[10] High NLR is an indicator of excessive neutrophil response and possible rapid progression of atherosclerosis.[11] A study done by Kaya et al showed that NLR may be used to stratify cardiac risks in patients with coronary artery disease.[12] Sönmez et al also showed that complexity and severity of coronary artery can be assessed by measuring NLR showing that higher NLR is an indicator of severe CAD[13]. A significant relationship was observed between high NLR and age, gender, diabetes mellitus and hypertension. The results of this study done in our local population are in accordance with the previous studies and suggest that high NLR in patients with ACS should be used an indicator of severe CAD and to offer more aggressive treatment options in these patients preferably in a tertiary care cardiac centre to reduce adverse cardiac events.

Table 1: Characteristics of Patients in ACS Grouped According to NLR.

Neutrophil to lymphocyte ratio (NLR)	Complications		Total	P value
	Yes	No		
High NLR	39	3	42	0.000
Intermediate NLR	40	9	49	
Low NLR	23	19	42	
Total	102	31	133	

Table 2: Association between Neutrophil to Lymphocyte Ratio and Adverse Outcome in Acute Coronary Syndrome

Clinical Characteristics	Low NLR n=42	Intermediate NLR n=49	High NLR n=42
Arrhythmias	2 (4.76%)	3 (6.122%)	22(52.38%)
Left ventricular failure	18(42.85%)	28 (57.14%)	19(45.2%)
Cardiogenic Shock	1 (2.38%)	2 (4.081%)	18(42.85%)
Pulmonary edema	0 (0.00%)	1(2.040%)	6(14.2%)
Ongoing ischemia	0 (0.00%)	7 (14.28%)	2(4.76%)
Thromboembolism	0 (0.00%)	2 (4.081%)	4(9.5%)

CONCLUSION

Neutrophil lymphocyte ratio (NLR) calculation by routine blood count examination is an easily measureable value and can be used as an indicator to assess risk of adverse cardiac events in patients with ACS with higher value posing increased risk of adverse events.

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ASSOCIATION OF DIABETES MELLITUS WITH HYPERTENSION AND ISCHAEMIC HEART DISEASE IN MALES AND FEMALES

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Abstract

Background: Diabetes mellitus has been known to coexist with both HTN (hypertension) and IHD (ischemic heart disease); though many times, only one of these is present in diabetics.

Objective: To assess association of diabetes mellitus with hypertension and ischemic heart disease.

Methods: This was a cross sectional study conducted on diabetes mellitus type 2 patients in outpatient department of Jinnah hospital, Lahore. 180 patients (93females and 87 males) were enrolled after fulfilling the inclusion criterion. They were assessed for the presence or absence of HTN and IHD.

After approval from ethical committee and informed consent from subjects, detailed demographic information was collected. Data was analyzed in Minitab version 17. Pearson Chi square test for independence was used to assess for the association of diabetes (in males as well as females) with HTN and IHD separately.

Results: The chi square statistic in first case was 0.362 (<3.84) and p value was 0.547 (not significant). In other words, no relationship (diabetes in females as well as in males with hypertension) could be found, whereas the corresponding values in other case were 11.376 (>3.84) and the obtained p value was 0.001 (highly significant). So, there was an association between diabetes (either in females or males) with IHD.

Conclusion: The results of the study have shown that diabetes is unrelated to hypertension in our patients, though it is associated with IHD. Further statistical analysis is required to specify whether relationship is present in males or females.

Key Words: Hypertension, IHD, diabetes mellitus

There are recommendations to support the increase in heart illness in diabetic patients as a result of coexisting illness, for instance, high blood pressure.[2]

High blood pressure exists most of the time even before diabetes appears for the first time. This suggests that high blood pressure is not dependent on it.[3]

Age on its own is the greatest hazard of mortality from causes related to heart and blood vessels as well as high blood pressure in bigger communities.[5]

Once dissimilarities in other hazards related to heart and blood vessels in both genders were standardized, comparative effect of diabetes on illness related to cardiac tissue and blood vessels in the periphery or CVA was similar in males and females, though in case of death from causes related to heart and vessels as well as when heart has failed, the effect is more in females.[11]

There is escalation in hardening of blood vessels due to atheroma in a direct manner as well by causing high blood pressure when there are high concentrations of serum insulin which occur in carbohydrate intolerance abnormalities, for instance, high blood pressure linked to DM 2 and increased adiposity.[15]

High serum glucose levels have role to play in the evolution of high blood pressure by retaining Na^{+2} and a rise in Na^{+2} which can be exchanged.[15]

Increased serum cortisol before noon was found in people who were intolerant to glucose, had

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high blood pressure as well as had deranged serum lipid levels.[16]

In the past, diabetes has been shown to be related to hypertension and ischemic heart disease. Our present investigation focusses on finding out whether it has got any association with either the former or the later separately in males or females in our study sample.

METHODOLOGY

180 subjects from the Diabetic clinic, Jinnah Hospital, Lahore city were examined. The design of study was cross sectional. The sample size of 180 subjects consisting of 93 females and 87 males (those fulfilling the inclusion criteria) was taken through non probability purposive sampling. Diabetes mellitus type 1, age less than 31 years and patients with severe complications were excluded. The study was approved by ethical review board of Jinnah hospital. Subjects were already diagnosed type 2 diabetics. They were labeled as "hypertensive", if either their blood pressure reading was 130-139/80-89 mm Hg,[13] they were on anti- hypertensive medications or they were diagnosed by a practitioner before. They were considered to be having ischemic heart disease (either angina, myocardial infarction or congestive heart failure) based on symptoms if they had chest pain on exertion, crushing pain even at rest or had breathlessness more on lying down respectively. Subjects were categorized on the basis of presence or absence of hypertension (HTN and non HTN) and ischemic heart disease (IHD and non IHD) in males and females separately. For statistical analyses, Minitab (version 17) was used. Pearson Chi square test for independence was used to assess for the association of diabetes in males as well as females with hypertension and ischemic heart disease separately. The value obtained by chi square statistic (for all the cells combined) was considered significant if it was above critical value of 3.84. The p-value (level of marginal significance) as was set at <0.05 and the degree of freedom was 1.

B.P. (Blood pressure) was taken when the subject was relaxed, had not taken tea as well as had not performed exercise in last half an hour. A standard mercury sphygmomanometer and a stethoscope were used for that purpose. B.P. was obtained first by palpatory method. First Korotkoff sound was labeled as systolic (B.P). When the Korotkoff sounds became muffled, that level was labeled as diastolic (B.P). Two readings were taken one minute apart with ±2 mm Hg error allowed.[14]

Mean age of total sample population (180 patients) was 47 years.

Out of a total of 91 (50.6%) patients with HTN, 45 (49.5%) were females and 46 (50.1%) were males; out of 89 (49.4%) who did not have HTN, 48 (53.9%) were females and 41 (46.1%) were males (chi square =0.362, p = 0.547). In other words, no relationship (diabetes in females as well as in males with absence or presence of hypertension) could be found. (Table no: 2)

Out of a total of 55 (30.6%) patients with IHD, 18 (32.8%) were females and 37 (67.2%) were males; out of 125 (69.4%) who did not have IHD, 75 (60.0%) were females and 50 (40.0%) were males (chi square =11.376, p = 0.001).So, there is an association between diabetes (either in females or males) with IHD (presence or absence). (Table no: 3)

DISCUSSION

Table 1: *Demographic and Clinical Profile of Patients*

Variable n=180	Frequency	Percentage
Age Mean = SD =		
< 50	85	47
> 50	95	53
Gender		
Male	87	48.3
Female	93	51.7
Hypertension		
Yes	91	50.1
No	89	49.9
IHD		
Yes	55	30.5
No	125	69.5

Table 2: Diabetes Mellitus Gender Distribution and Hypertension Cross Tabulation

Diabetes	HTN		Total
	No	Yes	
F (Females)	48 53.9%	45 49.5%	93 **51.7%**
M (Males)	41 46.1%	46 50.1%	87 **48.3%**
Total	89 100.0%	91 100.0 %	180 **100.0 %**
Chi-square P value	0.362 0.547		

The outcome from a study propose that high blood glucose levels alone in these individuals can explain hazard related to heart and vessels seen in people with diabetes in contrast with people without diabetes.[1]

Table 3: Diabetes Mellitus Gender Distribution and IHD Cross Tabulation

Diabetes (gender wise)	IHD		Total
	No	Yes	
F (Females)	75 60.0%	18 32.8%	93 **51.7%**
M (Males)	50 40.0%	37 67.2%	87 **48.3%**
Total	125 100.0 %	55 100.0 %	180 **100.0 %**
Chi- -square	11.376		
P value	0.001		

As compared to people without diagnosed diabetes, % age of individuals suffering from high blood pressure in an investigation was more among individuals who were already diagnosed with diabetes. The relationship of known high blood pressure and diabetes in males was as strong as that in the females.[2]

Out of the whole group of diabetic people investigated, blood pressure values of seventy-six and a half percent and 85.8 percent individuals were same or more than 130/85 and 130/80 mm Hg in that order, thus were hypertensive.[4]

New cases (per year) of high blood pressure in patients having non- insulin dependent diabetes mellitus were 7.8, 3.3 and 9.2 percent at 2, 5 and 7 years respectively, though these alterations had no statistical significance.

Diabetes and high blood pressure were more prevalent in Negroes than the non-black individuals or those of Spanish origin throughout every group of body mass index, though the statistical significance was not present in all dissimilarities.[7]

The susceptibility of females to sequels of diabetes on illness related to heart and blood vessels is greater as compared to that in males.[8] While comparing hazard of mortality from heart disease in men suffering from diabetes and those without diabetes after twelve years, it was found out that the former were prone to develop that hazard by three fold and this was independent of age, ethnicity, concentration of cholesterol, systolic B.P. and consumption of tobacco.[8]

Majority of investigations originating from community which inscribe diabetes as a nondependent hazard in males and females, recommend that coronary illness is predicted by diabetes in a superior manner in females as compared to males when other variables affecting the outcome are adjusted.[9]

Dissimilarity in men and women for death from ischemic heart disease lessened, if only diabetes existed at the outset, but no contrast in them was observed if both cardiovascular disease and diabetes existed at the outset.[10]

On the whole, the occurrence of new illness related to heart and blood vessels in males suffering from diabetes was about two times more as compared to that in normal males. For females suffering from diabetes, the occurrence of the same illness was about thrice that of females without diabetes.[11] As the person grows older, the effect of diabetes on the hazard related to CV illness decreases, especially in females.[(11)]

Sudden heart attack caused about ten percent of type two diabetics below fifty-five years to get admission, whereas, equivalent values for those between fifty-five and sixty-four years old were thirty five percent.[12]

As discussed before, effect of gender as well as age of onset of diabetes on incidence of CV illness should be assessed in prospective studies. Therefore, in our cross-sectional study, no inference can be made. In our study, in contrast to other investigations, relationship of diabetes was assessed with hypertension and ischemic heart disease without assessing other factors such as hypercholesterolemia, smoking, age at onset of diabetes, whether

diabetes occurred before or after hypertension or ischemic heart disease, control of diabetes itself, level of activity, education and socioeconomic status of patients.

CONCLUSION

The outcome of our investigation has shown that diabetes (in males or females) is associated only with ischemic heart disease, whereas it has no significant association with hypertension in either sex. Other factors known to affect the relationship of diabetes with their outcomes should have been assessed in our study as well.

RECOMMENDATIONS

People should be updated regarding the control of diabetes once it has occurred; moreover, complications of diabetes should be addressed.

LIMITATIONS OF STUDY

- Sample size was small
- No factor other than hypertension and ischemic heart disease was taken into account.
- Adjusted residuals were not analyzed, so it could not be inferred whether association of diabetes with IHD was in males or in females.

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SURGICAL DEBULKING AFTER SUPERSELECTIVE EMBOLIZATION OF EXTRACRANIAL ADVANCED HIGH FLOW VASCULAR MALFORMATIONS: OUTCOME BASED ON EXPERIENCE OF TWO CENTERS

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Abstract

Background: High flow vascular malformations are challenging lesions requiring multidisciplinary approach. Embolization and surgery, alone or in combination have been described as treatment modalities, yetstudies evaluating outcomeof combined approach are very few. We present the outcome after managing this pathology with super selective embolization followed by surgery and evaluate association of various variables with the outcome.

Material and Methods: This prospective descriptive case series was conducted from January 2009 to December 2018 in the department of Plastic and Reconstructive surgery Lahore General Hospital Lahore and Jinnah Burn and Reconstructive Surgery Centre Lahore. Patients of either gender between 15-50years with high flow Vascular Malformations in Shobinger stage 3 of any region were included. Patients with stage 1,2 or 4,intracranial extension or who were previously operated / embolized were excluded. Surgical debulking was done within 48 to 72 hours of embolization. Patients were followed monthly for24 months after surgery and outcome was assessed. Association of age, gender, duration, site and size of lesion with the outcome was analyzed.

Results: 32 patients were included in the study. Complete response was achieved in 16 (50 %) patients, partial response in 14 (43.7%) patients and 2(6.2%) patients had recurrence. Age, gender and site of lesion did not show any significant association with treatment outcome. While lesion size (p=0.000) and duration of disease (p=0.027) showed significant association.

Conclusion: Super selective embolization followed by resection within 48 to 72 hrshas excellent results in high-flow extra-cranial arteriovenous malformations.

Keywords: Outcome, Surgical management, Embolization, High flow vascular malformations.

High Flow Vascular malformations (VMs) are abnormal shunts between arteries and veins without intervening capillaries. They can arise anywhere in the body and have a wide range of presentations.[1] These lesions are present at birth in 40% of the cases, with mostly arteriovenous malformations (AVMs) and clinical course is followed according to Schobinger clinical staging system.[2,3]

High flow Vascular Malformations are direct fistulous connections with an intervening convoluted network of blood vessels having poorly differentiated endothelial cells.[4] Over time, the lesion continues to expand leading to skin changes, bleeding, ulceration and tissue necrosis. If left untreated high flow into the venous system gradually leads to volume and pressure overload within the heart and

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subsequent heart failure.[5] For management of the lesion, natural history, appropriate diagnostic studies, selection of treatment option is required for long term results.

Treatment of High flow Vascular Malformations depends on severity of symptoms and lesion location. Patients with Schobinger stage I and II are managed conservatively with regular follow up. Surgical intervention is required for stage III lesions, with grade IV lesions needing treatment of heart failure, followed by intervention. Embolization alone or in conjunction with surgical resection is described as the primary treatment option for high flow vascular malformations now a days. This results in least recurrence rate, decreased blood loss during surgery and less mutilation of tissues as in case of surgery alone. The goal of embolization is to occlude the nidus and to prevent the formation of collateral flow.[6] However, if not followed by surgical debulking, collaterals start to develop, resulting in recurrence and more complex feeding pattern to the nidus.

Super selective embolization, which targets the closest vessel feeding the nidus, ensures complete disruption of flow to the nidus and prevents unnecessary disruption of blood flow to the important organs. Embolization and surgical debulking within 48-72 hours has resulted in best outcome yet, with least recurrence.[7] As compared to high flow vascular malformations in extremities where tourniquet can be applied, those presenting in head and neck present a unique challenge and super selective embolization offers a leap forward in the management of these lesions. Nevertheless, embolization can be done in all regions due to its various benefits as mentioned above.

In a large case series done by Wang in 2015 it was noted that high flow Vascular Malformation resolved completely in terms of devascularization in 56 (84.8%) cases and partially in 10 (15.2%) cases who underwent embolization.[8] Pompa showed excellent results in 7 patients (35%) good results in11 (55%), satisfactory in 2 patients (10%) who underwent surgical excision after embolization.[9] Another larger series by Catarina Oliveri are ported a partial response rate in 64.3% and complete response in 14.3% while recurrence in 21.4% of patients.[10]

Thus there is not only variability in the already published literature about management and the outcome of high flow AVM, but also the association of age, gender, duration, site and size of lesion with the outcome has been poorly documented. Thus we did this case series not only to determine the outcome of surgical resection after embolization in high flow VMs, but also to analyze the association with various variables.

METHODOLOGY

This is a prospective descriptive case series conducted from January 2009 to December 2018 in the department of Plastic and Reconstructive surgery Lahore General Hospital Lahore and Jinnah Burn and Reconstructive Surgery Centre Lahore. We included patients of either gender between 15-50 years with high flow Vascular Malformations in Shobinger stage 3 of any region. Shobinger stage III malformation was defined clinically as a pulsatile and expanding swelling with bruit / thrill and either ulceration, pain or bleeding from the lesion. It was confirmed through contrast enhanced MRI. Patients with stage 1 or 4 lesion, intracranial extension or who were previously operated / embolized were excluded. After informed consent, patients were enrolled for the study and all the clinical findings were recorded. After determining fitness, patients underwent super selective embolization of the lesion. This was followed by surgical debulking within 48-72 hours. Surgical debulking consisted of excision of nidus and debulking of the tissues on subunit principle by taking contralateral side if available as template. Reconstruction was done by primary closure, redraping the local skin flap after debulking in case the skin was not involved or with regional flaps if the local tissues were not reusable. Figure 1 shows patient who had high flow vascular malformation of forehead and was treated with super

selective embolization and debulking. Patients were discharged, and subsequently followed on monthly bases for 24 months after the surgery. Outcome was assessed on follow up and subsequent surgery was planned after workup. Compete response of the treatment was considered if the lesion specific symptoms like pain, swelling or functional disability were completely resolved after surgical resection. Recurrence was considered if the lesion specific symptoms remained unchanged after surgical resection. Partial response was considered if lesion specific symptoms fell in between complete response and recurrence after surgical resection. The data analysis was subsequently analyzed. Mean and standard deviation were calculated for quantitative variable like age and duration of disease. Frequency and percentage was calculated for qualitative variable as gender and outcome. Effect modifiers were controlled through stratification. Stratification was done for age and duration of disease, size of lesion, and site of lesion. Post stratification, chi–square test was applied by taking P ≤0.05 as significant.

RESULTS

A total of 32 patients were included in this study. Mean age of patients in this study was 24.84± 6.63 years. Minimum and maximum age of patients was 15 and 47 years.14 (43.7%) patients were male, while most patients, i.e 18 (56.3%) were female. Mean size of the lesion was 14.15±7.23 cm. with a minimum of 4cm and maximum size noted was 25cm.Involvement of the areas were as follows: Cheek 6 (18.7%), ear 3 (9.4%), forearm 4 (12.5%), forehead 7 (21.9%), lip 4 (12.5%), eyelid 1 (3.1%) and scalp 7(21.9%). Outcome showed complete response in 16 (50%) patients, partial response in 14(43.7%) patients and 2(6.2%) patients had recurrence. Stratification of data was then done according to age, gender, duration, site and size of the lesion. No statistically significant difference was observed for treatment outcome with regard to age(p=0.217), gender (p=0.429) and site of the lesion (p=0.118). On the contrary, shorter duration of diseases was significantly associated with treatment outcome. i.e. p value = 0.027.Similarly, size of lesion was significantly associated with treatment outcome. i.e. p-value=0.000.

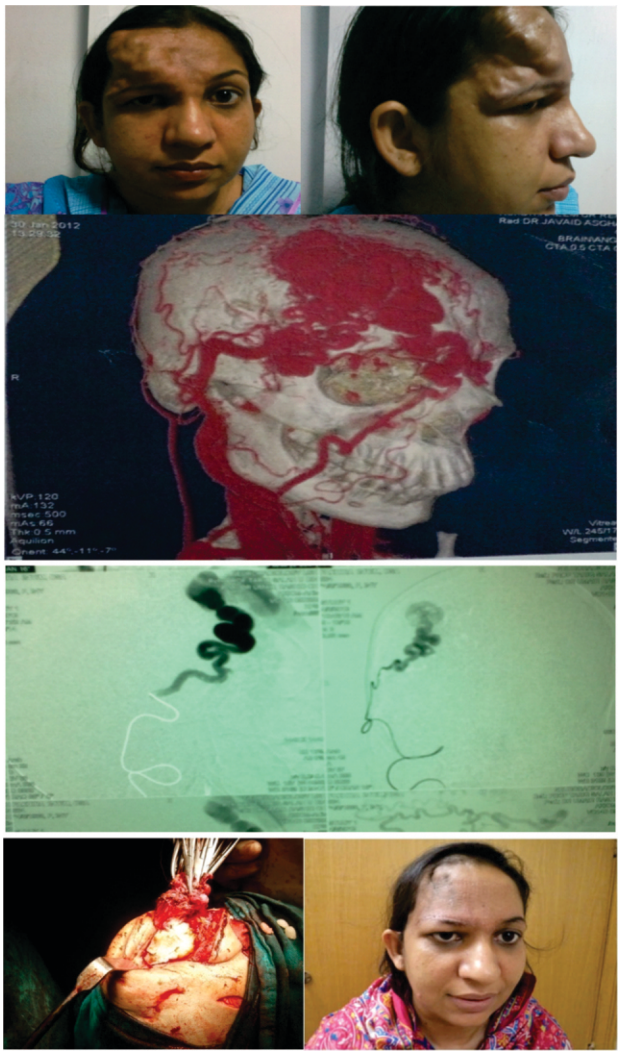

Figure1: *24 Years Old Female Presented with High Flow Extra Cranial Vascular Malformation of forehead. Superselective embolization was done by catheterizing superficial temporal artery. Surgical debulking after 48 hours resulted in excellent outcome.*

DISCUSSION

Extracranial arteriovenous malformations can cause tremendous cosmetic, functional, and psychological problems. Small and superficial AVMs canbe cured by surgical resection, most AVMs are inoperable as they are large and diffuse in nature and they

involve important adjacent structures.[9] With improvements in catheter technology, super selective techniques and the use of liquid embolic agents, embolotherapy has emerged as a significant modality for treatment of the high flow vascular malformations.[9,11]

One of the greatest in conveniences of surgery as a primary modality is its mutilating factor, which is particularly important in face. Embolization is not only a complementary but also an alternative treatment, especially in infltrative cases with a higher surgical risk of bleeding and mutilation. The transarterial and the percutaneous route are the most common approaches used in this type of injury: the percutaneous approach, associated with a higher rate of complications, but is reserved when it is not possible to catheterize the nutrient artery.

In this study treatment outcome of embolization followed by surgical resection of patients showed that 16 (50%) patients had complete response, 14(43.7%) patients had partial response and 2(6.2%)patients had recurrence. Su Lu in his large case series reported complete resolution in terms of devascularization in 56 (84.8%) cases and partially in 10 (15.2%) cases who underwent embolization.[8] While Pompa V in his study reported very good results in 7 (35%), good in 11 (55%) and partial in 2 (10%) cases who underwent surgical procedure with embolization.[9]

Results of our study are comparable with findings of studies done by Su Lu and Pompa V. Another larger series reportedby Da Resposta showed partial response rate in 64.3% and complete response in 14.3% while recurrence occurred in 21.4% of patients.10Complete response reported by Da Resposta is lower when compared the results of our study for complete response after treatment.

The treatment of choiceis the selective embolization of vessels in combination with surgical resection and reconstruction of the soft tissues.[12] The aim of preoperative embolization is mainly to reduce blood loss and facilitate the surgery and must not be considered a method for reducing the extent of resection. Surgical resection should not be delayed beyond 48 hours after embolization because the resulting inflammation renders the aforementioned hemodynamic benefits useless and the surgery become more difficult.[12,13,14]

The aim of embolization is to block the high-flow shunt between the arterial and venous systems. The reduction or closing of AVMs renders resection and surgery more accurate, safer, and easier. The potential risks associated with extra-axial embolization include the neurological defects caused by the reflux of the material occluding the intra-axial vessels that supply blood to the brain and the possible paralysis of cranial nerves caused by the closure of the small vessels of the external carotid artery supplying the cranial peripheral nerves. However, these complications are rare and are minimized by the experience of the operator and when superselective embolization is done.[12,13,14] It is essential that these procedures are performed in specialized centers, where there are clinicians with appropriate skills. The introduction of the direct flow embolization technique and a better understanding of the principles of flow and occlusion have significantly lowered complication rates.

There are reports in the literature of high success rates for head and neck AVMs by single-modality treatment particularly embolization.[13,15,16] It is known that after embolization alone collateralization and new vessel recruitment can occur allowing the lesion to expand and infiltrate adjacent normal tissue. The reported cure may be secondary to limited follow-up periods. Also, the term cure varies in the literature. Some use the term to indicate an asymptomatic state after embolization, not necessarily the absence of disease. The management of head and neck AVMs requires multi disciplinary and multi modality care by appropriately trained physicians.[17,18] Treatment requires repeated therapy for disease control. The overall goal of treating AVMs is to selectively manage the vessels involved. Afterwards, surgical resection of the nidus and debulking of the rest of the tissues offers best outcome in terms of reduced recurrence. With this approach, management of head and neck AVMs is definitely possible as indicated in our study. Untreated lesions without

expectation will cause significant morbidity in time as not only the rate of growth is unpredictable, but the delay results in poor outcome as indicated in our case series.

CONCLUSION

Results of this study showed that combined super selective embolization and resection / debulking results in good cure rate for high-flow extracranial vascular malformation. It is also recommended that the extra-cranial vascular malformation should be assessed carefully by a team consisting of plastic surgeon and interventional radiologist, asa combined treatment protocol consisting of super selective embolization followed by total resection, ideally carried out within 48-72 hours ensures the best possible outcome.

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EVALUATION OF COMPARATIVE EFFECTS OF THREE IRON CHELATION THERAPIES AMONG BETA-THALASSEMIA MAJOR PATIENTS IN LAHORE, PAKISTAN

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Abstract

Objective: To observe the effect of iron chelation therapy oral, parenteral and combination in thalassemic patients

Study Design: Descriptive study

Methods: 75 patients below age 12 randomly recruited from Sundas Foundation Lahore, Sir Ganga Ram Hospital Lahore & Children's Hospital, Lahore. Both males & females diagnosed with thalassemia and having the iron chelation therapy oral, subcutaneous or combination was included in the study. Detailed history and different parameters were observed and entered into the specifically designed data collection form. Complete history, diagnosis, management, side effects of medication & clinical manifestations were noted in data form. Patients were categorized into 3 groups; Group I included n=25 receiving oral iron chelator Deferiprone, Group II included n=25 receiving subcutaneous Desferrioxamine injection and Group III included n=25 getting regular oral Deferiprone and subcutaneous Desferrioxamine. Data obtained from data collection form was analyzed by using SPSS 20.0.

Results: Among 75 thalassemic patients included in study, there were 74.6 % (56) males and 25.3% (19) were females. There were 88% patients suffering from thalassemia major in Group I, while among Group II & III thalassemia major patients were 84% & 80% respectively. Total number of annual blood transfusions was categorized into 3 categories: category 1 included patients having up to 5 transfusions, category 2 had 6-10 transfusion, and category 3 included 11 - 20 transfusions.

Side effects of oral iron chelation therapy in Group I were gastrointestinal symptom and bone changes in 28% & 12 % respectively while 60 % didn't reported any side effect. Among Group II & III, nausea and gastrointestinal symptoms were 36% and 44 % respectively. Injection site lump infection was reported in 28% & 20% patients of Group II & Group III, Skin rashes were reported in 28% & 20%, bone changes were 20% & 16 % in Group II & Group III respectively. While 20% & 12% patients didn't reported any symptoms or side effects among Group II & Group III respectively. With therapy, decrease in serum iron level was 30%, 50% & 70% in Group I, II & III respectively. Patient compliance was highest for Group III, 92%. Among patients of Group I & II, compliance was 76% & 88 % respectively.

Conclusion: In conclusion, intensive chelation therapy using combined Desferoxamine (DFO) and Deferiprone (DFP) appears to be more efficacious than each of these agents in isolation due to the additive/ synergistic effect. Our data on patients receiving intensified combined chelation therapy suggests that it has a more positive impact on patients' quality of life by reducing ferrit in and total body iron to normal levels as compared to either therapy alone

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The most common worldwide human monogenic disorders are inherited syndromes of hemoglobin (Hb) generation, amongst which clinically substantial are those poignant to the adult β globin gene (HBB) – sickle cell disease (SCD) and β thalassemia.[1] Thalassemia disorders are a heterogeneous assembly of hemoglobin disarrays because of a diminished or missing production of typical globin chains.[2] Beta-thalassemia is predominant in Southeast Asia, southern China, and Mediterranean countries. In Pakistan, the incidence of thalassemia carriers is seen in 7 to 10 million individuals (5-8%).[3] Subtypes of thalassemia are: β-thalassemia major (TM); β-thalassemia intermedia (TI); and thalassemia minor. Patients with TM usually presents at the age of 6-24 months; with pallor, feeding problems, recurrent episodes of fever, enlarged abdomen and failure to thrive, requiring consistent blood transfusions for survival.[4] Skeletal abnormalities in beta thalassemia major include expanded bone marrow space resulting in thinning of the bone cortex. These changes are particularly obvious in the skull which shows the characteristic "hair-on-end" appearance. Bone changes of the facial bones are also very obvious.[8]

The consequence of regular blood transfusions is excess iron absorption i-e about 200-250 mg iron during each blood transfusion[5]. Tissue damage and fibrosis result due to accretion of the lethal amounts of iron. The liver and biliary tract of thalassemia major patients may show evidence of extramedullary hematopoiesis and damage secondary to iron overload from multiple transfusion therapy.

The heart is a major organ affected by iron overload and anemia. Cardiac dysfunction in patients with thalassemia major includes conduction system defects, decreased myocardial function, and fibrosis. Some patients also develop pericarditis. Cardiac magnetic resonance imaging (MRI) is considered the criterion standard for measuring cardiac indices, as well as for evaluating cardiac overload by measurement of T2* (relaxation parameter), with a cardiac T2* of less than 10 ms being the most important predictor of development of heart failure.[9]

To elude the complications of iron overload, constant iron chelation therapy (ICT) is crucial. (6) The three commonly used iron chelators are: Desferoxamine (DFO), Deferiprone (DFP) and Deferasirox (DFX). Parenteral desferoxamine has been successfully utilized with oral deferiprone or deferasirox.[6] All iron chelators help in decreasing the organ iron content and serum ferritin levels. The choice of iron chelator depends upon many variables including patient preference, compliance of patient, cost and efficacy of iron chelator. The main purpose of ICT is to sustain iron equilibrium in transfusion-dependent patients and to evade complications due to iron overload rather than curing the disease.[5] Thalassemia minor usually presents as a mild, asymptomatic microcytic anemia and is detected through routine blood tests in adults and in older children. These laboratory findings should be evaluated as indicated.

While the effectiveness of individual iron chelation therapies has been thoroughly investigated, there is limited comparative information about the combined benefits of the therapies. The aim of the study was to compare the effects of oral, parenteral iron chelators and their combination in the management of iron overload in thalassemic patients and to compare the dose, dosage regimen and cost of oral, parenteral iron chelators and combined oral and parenteral iron chelators in local thalassemic children population.

METHODOLOGY

A descriptive study was conducted to observe the effect of iron chelation therapy oral, parenteral and combination in thalassemic children. We recruited the 75 patients below age 12 randomly from Sundas Foundation Lahore, Sir Ganga Ram Hospital Lahore & Children's Hospital, Lahore. We included both males & females diagnosed with thalassemia and having the iron chelation therapy oral, subcutaneous or combination. Detailed history and different

parameters were observed and entered into the specifically designed data collection form. Complete history, diagnosis, management, side effects of medication & clinical manifestations were noted in data form. Patients were categorized into 3 groups; Group I included n =25 receiving oral iron chelator Deferiprone, Group II included= 25 receiving subcutaneous Desferrioxamine injection and Group III included n = 25 getting regular oral Deferiprone and subcutaneous Desferrioxamine. Data obtained from data collection form was analyzed by using SPSS 20.0.

RESULTS

Among 75 thalassemic patients included in study, there were 74.6 % (56) males and 25.3% (19) were females. In Group I, 36 % patients have positive family history of thalassemia while 64 % have no family history. For Group II & Group III, 56% & 40% patients have positive family history respectively.

There were 88% patients suffering from thalassemia major in Group I, 12 % suffered from thalassemia intermedia while among Group II & III thalassemia major patients were 84% & 80% and thalassemia intermedia patients were 16% & 20 % respectively.

Following table shows the lab investigations done for diagnosing the thalassemia patients. Percentages of different tests performed among three groups are as follow:

Thalassemia patients presented with following common sign and symptoms; anemia, fatigue, growth retardation, facial growth deformities (chipmunk faces) and pale skin. Table below shows the percentages of these signs and symptoms among patients of three groups.

Table 1:

Methods of Diagnosis	Group I	Group II	Group III
CBC & Blood Smear	81%	56%	69%
Iron studies including serum iron, ferritin, unsaturated iron binding capacity (UIBC), total iron binding capacity (TIBC), and percent saturation of transferrin	10%	2%	3%
Hb Electrophoresis	11%	32%	2%

Treatment for thalassemia patients is blood transfusion with frequency determined by individual needs and bone marrow transplant. In our study, the mainstay of treatment was blood transfusion; in group I, 95 % patients received blood transfusions, in group II, 97% & in group III, 99 % patients received blood transfusion while bone marrow transplant was done for 5% patients in group I, 3% in group II and 1 % group III.

Table 2:

SYMPTOMS	Group I	Group II	Group III
Anemia	100%	100%	100%
Fatigue	86%	72%	80%
Growth Retardation	66%	72%	80%
Facial Bone Deformity	28%	8%	20%
Skin Pallor	54%	40%	60%

Total number of annual blood transfusions was categorized into 3 categories: category 1 included patients having up to 5 transfusions, category 2 had 6-10 transfusion, and category 3 included 11 -20 transfusions. Group I comprised of 80 % patients falling in category 1, 12 % in category 2 and 8 % in category 3. For Group II, 64% were in category I, 28 % were in category II and 8 % in category 3 while the 52% patients of Group III were in category 1, 32% were in category 2 and 16% were in category 3.

Side effects of oral iron chelation therapy in Group I were gastrointestinal symptom and bone changes in 28% & 12 % respectively while 60 % didn't reported any side effect.

Among Group II & III, nausea and gastrointestinal symptoms were 36% and 44 % respectively. Injection site lump infection was reported in 28% & 20% patients of Group II & Group III, Skin rashes were reported in 28% & 20%, bone changes were 20% & 16 % in Group II & Group III respectively. While 20% & 12% patients didn't reported any symptoms or side effects among Group II & Group III respectively.

With therapy, decrease in serum iron level was

30%, 50% & 70% in Group I, II & III respectively. Patient compliance was highest for Group III, 92%. Among patients of Group I & II, compliance was 76% & 88 % respectively.

DISCUSSION

Thalassemia major patients require a regular transfusions resulting in iron overload as human body is deficient in a contrivance to excrete surplus iron. Transfusional hemosiderosis results in many complications that can be averted and to some extent, regressed by sufficient iron chelation.[4] In the present study, the combined therapy of deferiprone with deferoxamine was found to be the most efficacious as it decreases the iron burden and serum ferritin levels significantly. These results are in covenant with those of Balveer, et al.[10] and Sharma, et al.[11] in obviating the complications of iron overload.

Side effects of oral iron chelation therapy in Group I were gastrointestinal symptom and bone changes in 28% & 12 % respectively while 60 % didn't reported any side effect. GI complications were reported in 23 % & arthropathy was reported in 7.69% patients in a study reported by Ayyub et al.[16]

The present study revealed following side effects in group II & group III i.e. Lump infection at injection site, bone changes, GI disturbances and skin rashes in patients of thalassemia major and these side effects were reported more among group II than group III (combined DFO + DFP). Our results were consistent with Borgna and Marsella.[12]

The complications of thalassemia iron chelation therapy like stunted growth and bone changes were more frequently observed in patients receiving DFO and DFP alone (group I & II) as compared to group III, as studied by Mobbara, et al.[13]

The combination therapy escalates the efficacy of treatment and does not intensify the menace of adverse effects from either chelator. As suggested by the shuttle hypothesis, the synergistic effect of DFP and DFO on negative iron balance resulted in an improved iron chelation with a magnitude indistinguishable to the acceleration in the dose of DFO.[14]

Patient compliance was highest for Group III, 92%. Among patients of Group I & II, compliance was 76% & 88 % respectively. Dual chelation therapy regimen is more effective, less toxic and well tolerated in comparison to either drug alone. Same result was reported by Badr et al.[17]

This study revealed that patients with combination therapy (group III) were more compliant to treatment due to least side effects, short duration of therapy and the cost of subsequent treatment was not ominously different from that of DFO or DFP alone rather it was less expensive as compared to monotherapy of both drugs (group I and II) as studied by Maggio, et al.[15] ultimately improving the quality of life and life expectancy of patients with thalassemia major.

In conclusion, intensive chelation therapy using combined DFO and DFP appears to be more efficacious than each of these agents in isolation due to the additive/ synergistic effect. Our data on patients receiving intensified combined chelation therapy suggests that it has a more positive impact on patients' quality of life by reducing ferritin and total body iron to normal levels as compared to either therapy alone.

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DESCRIPTIVE STUDY OF ORAL MANIFESTATIONS AND MANAGEMENT OF FLUID ELECTROLYTE IMBALANCE IN CHRONIC KIDNEY DISEASE PATIENTS ON DIALYSIS

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Abstract

Objective: To observe the management of electrolyte imbalance in hemodialysis (HD) patients as well as oral manifestations if any present among these patients

Study Design: Descriptive study

Methods: 50 patients belonging to different age groups were selected randomly from dialysis unit of Jinnah hospital, Lahore; their detailed history and different parameters were observed and entered into the data collection form. Both male and female were included who had history of chronic kidney disease (CKD), end stage renal disease (ESRD), continuous abdominal peritoneal dialysis (CAPD) and undergoing HD treatment. Adata collection form was developed to obtain complete history, diagnosis, management, side effects of medication and clinical manifestations; this form was filled by directly interviewing the patients and also from the nurses and physicians. Oral findings were noted by doing the detailed oral examination.

Results: Among the 50 patients selected, 44 % of them suffered CKD due to hypertension, 30% because of diabetes, 6% had physical injury, 12 % had renal stones & 8% had other causes. Only 20 % had weight gain issue. Among patients undergoing dialysis, 20% suffered from fluid retention and presented with edema. Majority of dialysis patients had normal serum sodium (Na) levels, whereas 20% suffered from hypernatremia and 16% from hyponatremia. Hyperkalemia was observed in 18% and hypokalemia in 8% patients. Hypocalcemia was observed in 10% patients & 12% suffered from hypercalcemia. Hyperphosphatemia was seen in 90% whereas hypophosphatemia in 4% patients & normal PO4-2 serum level was found in 6% patients only. The hemoglobin level in dialysis patients was maintained within normal levels by use of erythropoietin products in 70% cases, iron sucrose in 70%, vitamin B12 supplements in 20% & multivitamins and iron products in 10% cases. Among 50 patients, 33 presented with oral manifestations like uremic fetor, unpleasant taste, xerostomia, burning sensation, dry fissured lips, candidiasis, gingival hyperplasia and angular cheilitis.

Conclusion: Chronic kidney disease has become a major concern in public health worldwide and number of patients needing a kidney transplant is increasing. The oral rehabilitation of renal patients is complexed by systemic effects of renal failure, specially; anemia, bleeding problems, cardiovascular diseases or endocrine disturbances. Dental management can be performed by following a treatment protocol designed after discussing and coordinating with the nephrologist. Patients should be treated by keeping in view all systemic effects correlated to kidney dysfunction and scheduled follow-up should be maintained. Early diagnosis of oral and dental pathologies, good prophylaxis and patient education have central role in management.

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Kidney is the vital organ of human body which regulates the electrolyte and fluid balance by filtering waste, excess fluid, and toxins from blood. Kidney Failure occurs, when one develops End Stage Renal Disease (ESRD) or Chronic Kidney Disease (CKD); usually by losing kidney function about 85-90 % and Glomerular Filtration rate (GFR) becoming <15. Causes of CKD include; type I & II diabetes, raised blood pressure, glomerulonephritis, polycystic kidney disease (PKD), autoimmune diseases affecting the kidneys, urinary tract obstruction etc. (Dhondup & Qian, 2017).

Hemodialysis (HD) and peritoneal dialysis (PD) are renal replacement therapies. Tight control of electrolyte imbalance is very important for dialysis patients (Galli et al., 2011). Regulation of fluid and electrolytes in the HD and PD patients is a challenge; complications develop when balance is not maintained. Ultra-filtration impacts on fluid status in both HD & PD. By knowing the pathophysiology involved in fluid electrolyte imbalance occurring in ESRD, proper management can be carried out with medication, changes in diet and dialysis to provide patients with the best suitable renal replacement therapy (Nanovic, 2005; Venkat, et al., 2006).

The success of HD & PD therapy is affected by nutrition status. Malnutrition is one of the major factors in mortality & morbidity of dialysis patients. Insufficient intake of energy and protein supply, amino acids loss because of dialysis, the uremic state of metabolism, catabolic stress and endocrinological diseases are the causes of malnutrition. For effective long-term dialysis, anabolic nutritional state of the patients should be maintained (Schmicker, 1995).

Oral cavity mirrors the systemic health. Chronic renal failure (CRF) has spectrum of oral presentations, either because of disease or treatment. Oral presentations associated with chronic renal failure and with therapy are vast and include altered taste (in uremic patients, metallic taste is due to urea component and its breakdown products by bacterial urease i.e. ammonia and carbon dioxide) (Pontes et al., 2018).

Altered taste can also be because of following; metabolic disturbance, medication, reduced no. of taste buds and changed salivary composition & flow. Following oral findings have also been found in association with CRP & ESRD; gingival hyperplasia, xerostomia, loss of lamina dura, periodontal destruction, tooth mobility, mucosal lesions like candidiasis, ulcerations, angular cheilitis, hairy leukoplakia, lichenoid reactions etc. (Kuravatti, et al., 2016).

In uremic stomatitis there are markedly raised serum levels of urea and nitrogenous wastes in chronic renal failure patients. Clinically, it presents as white plaques most commonly on buccal mucosa, floor of mouth and tongue. Common complaints by the patients are pain, altered taste, burning sensation of oral mucosa. Ammonia or urea odor can be detected in the patient's breath (Gupta et al, 2015).

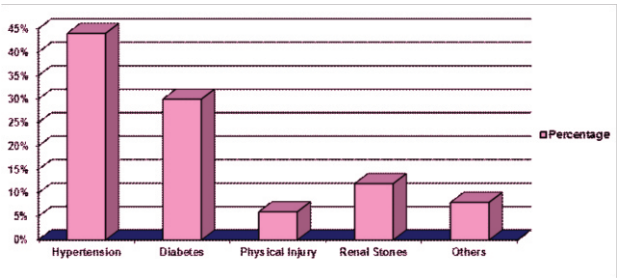
METHODOLOGY

The study was conducted to observe the management of electrolyte imbalance in HD patients as well as oral manifestations if any present among these patients. 50 patients belonging to different age groups were selected randomly from Dialysis unit of Jinnah Hospital, Lahore; their detailed history and different parameters were observed and entered into the data collection form. We included both males & females who had history of CKD, ESRD, CAPD and undergoing HD treatment. A data collection form was developed to obtain complete History, diagnosis, management, side effects of medication & clinical manifestations; this form was filled by direct interviewing the patients and also from the nurses & physicians who play a major role in management of these electrolytes. Oral findings were noted by doing the detailed oral examination. Data obtained from data collection form was analyzed by using SPSS 20.0.

RESULTS

Among the 50 patients selected, 44% of them

suffered CKD due to Hypertension, 30% because of Diabetes, 6% had Physical Injury, 12% had Renal Stones & 8% had Others causes.



Graph: *Causes of CKD in Dialysis Patients*

Majority of Patients didn't complain of weight gain during dialysis session only (20%) had weight gain issues; weight is usually controlled within target weight by Increasing Ultra filtration rate of dialysis (100%), Diuretics used (100%) & Modifications in Dietary Intake.

Among patients undergoing Dialysis, 20% suffered from fluid retention and presented with edema. Edema was managed by decreasing fluid/water intake, increasing ultra-filtration rate (UFR) & by diuretics & by decreasing intake of leafy vegetables in 40 % patients, decreased intake of fruits, decreased protein diet in 30 % patients. (table 1)

Patient's body weight was regulated by regulating the body water/fluid retention & it was managed by reducing water/fluid consumption in all patients, by increasing UFR in 80% & by dietary intake changes in 77% patients.

Dialysis patients' water intake was regulated and controlled by following these instructions; 90% patients were allowed to take just 1-2 glasses of water/day, only 10% patients were allowed to take more than 2 glasses/day, 80% were asked to avoid salty food, 30 % were asked to rinse mouth with water to deal with dry mouth, 70 % were using small using cups/glass & sucking small ice cubes for psychological satisfaction.

Majority of Dialysis patients had normal serum sodium (Na) levels, whereas 20% suffered from Hypernatremia & 16% from Hyponatremia.

Among the dialysis patients suffering from Hyponatremia; most patients show symptoms of hypotension during dialysis, 50% showed symptoms of muscle twitching & weakness & 25% complained of nausea & vomiting. Hyponatremia in patients was solely controlled by increasing the influx of Na in dialysis fluid going into the patient's body.

Folllowing sympotoms were observed in dialysis patients suffering from hypernatremia: Hypertension in 96 %, thirst Increase in 84%, weight gain & pitting edema was observed in 12% patients. It was managed by following medications listed in the following table 2.

Hyperkalemia was observed in 18% & hypokalemia in 8% patients. Hyperkalemia was managed by avoiding K-rich diet & K-supplement; Medical therapy included I.V Ca in 55 % patients, Oral K-xelate (15mg/dose) among 44%, 25% Dextrose water + Insulin among 55% & Diuretics were administered to 90 % patients.

Patients suffering hypokalemia had symptoms

Table 1: *Signs of Edema in Dialysis Patients & its Management*

Edema			Management of Edema						
	YES	NO	Decrease Water intake	Decrease Leafy Veggies intake	Decrease Intake of Na salt	Decrease Intake of fruits	Decrease Intake of Protein Diet	Increase UFR	Diuretics
%age	20%	80%	100%	40%	100%	20%	30%	100%	100%

Table 2:

Management					Medical therapy				
	Peppermint chew gums	Vit C lozenges	Na intake	Na influx in Dialyzing fluid	Hydralazine	Minipress	Herbessor	Diuretic	Other
%	0	0	100%	100%	80%	60%	40%	90%	60%

such as muscle weakness/fatigue & leg cramps. Nausea/vomiting & abdominal cramps were reported in 75 % patients & 22 % suffered from arrhythmia or cardiac arrest. Hypokalemia in Dialysis patients was solely (100%) treated with I.V Saline +K-Injection given during Dialysis.

Majority of patients had normal serum Ca levels maintained during Dialysis; however 10% suffered hypocalcemia & 12% hypercalcemia. Hypocalcemia symptoms twitching & cramping were observed in 60% patients, anxiety and irritability in 20 % & laryngospasm in 20 % patients. Hypocalcemia was managed by following measurement s tabulated here; (table 3)

Major symptoms observed in dialysis patients suffering from hypercalcemia included drowsiness, lethargy & headache in 80%, muscle weakness in 80%, bone pain in 60% & anorexia, vomiting, dehydration among 20%hypercalcemic patients.

Hypercalcemia management involved decreased intake of dairy products & decreased intake of Ca rich diet. Medications used included calcitonin in 20 % & bisphosphonate therapy in 80% patients.

Hyperphosphatemia was observed in 90% whereas hypophosphatemia in 4% patients & normal PO4-2 serum levels were found in 6% patients only.

Major symptoms observed for hypophosphatemia were muscle weakness in 90% & tremors in 10% patients.

Hpophosphatemia was managed by avoiding Phosphate binders in all patients & intake of high phosphate diet in 50% patients. Medications used were phosphate supplements in all hypophosphatemic patients & Vit-D supplements in 50% patients.

Major symptoms in Hyperphosphatemia cases were tetany or cramps observed in 75% patients. Hyperphosphatemia was managed by avoiding high Phosphate diet, avoiding Vit-D. Medications given in our study included Aluminium or Calcium containing Phosphate Binders in 33% cases, Non Al or Ca containing Phosphate binders in 66% & Diuretics in 99% cases.

The Hemoglobin levels in Dialysis patients was maintained within normal levels by use of Erythropoietin products in 70% cases, Iron sucrose in 70%, Vit B12 supplements in 20% & Mutli-Vitamin & Iron product in 10% cases.

Among 50 patients, 33 presented with following oral manifestations tabulated here; (table 4)

DISCUSSION

There are several causes of kidney failure or kidney dysfunction, Hypertension was the major cause to be observed in CKD patients in our study, while Diabetes, Renal stone, Physical or the Chemical injury were other causes for CKD. During dialysis, 20% of the HD patients gained weight. Weight gain was managed by medication and by increasing the Ultra filtration rate. Decreasing dietary intake also played significant role. 80 % of HD patients showed signs of edema i.e. swelling and puffiness of eyelids, hands and feet, and was managed by use of diuretics, less water intake and less sodium intake as well as by increasing ultrafiltration rate.

To control thirst in HD patients, 87 % patients were directed to avoid salty food, 70% patients used small cups or glasses, 10% patients used ice cubes

Table 3:

	Management			Medication		
	Dec. Intake of Phosphate	Inc. Intake of Dairy products (Milk, Yogurt)	Dec. Intake of Bisphosphonates	Oral Vit D_3 Supplement (Bonky, BonOne)	Oral Ca Preparation (Qalsan-D)	I.V Ca
%age	60%	60%	80%	60%	30%	10%

Table 4:

	Uremic fetor	Unpleasant taste	Xerostomia	Burning sensation	Dry fissure lips	Candidiasis	Gingival hyperplasia	Angular Cheilitis
%age of pts	63.63	60.60	72.72	51.51	27.27	9	15.15	36.36

and 30 % patients' rinsed mouth with water. In 16 % of HD patient's, hypernatremia occurred which caused hypertension, muscle twitching and weakness. 20 % of patients suffered from Hypernatremia which resulted in Hypertension in 96 % of HD patients and increased thirst in 84 % of HD patients. Excessive weight gain and pitting edema were also the consequences of hypernatremia but in 12% and 6% of HD patients respectively. These symptoms were managed by decreased sodium intake both in diet or dialyzing fluid. To control hypernatremia, diuretics 90%, Hydralazine 86%, minipress 60% and harbessor 40% were used.

Out of 50 HD patients, 8% patients suffered from hypokalemia which resulted in arrhythmias, cardiac arrest, leg cramps, muscle weakness and fatigue. Leg cramps and muscle fatigue were the major symptoms which were best managed by IV saline +K injection. 18 % of HD patients showed hyperkalemia which resulted in abdominal cramps. These symptoms were best managed by avoidance of K-rich diet and also K-supplements. Medications prescribed were loop diuretics 90%, oral K-xelate 44% and I.V Ca in 55% of HD patients.

Rate of occurrence of hypophosphatemia in HD patients was 4% which resulted in muscle weakness and tremors that was treated by use of diet containing high Phosphate contents and by avoiding Phosphate binders. Phosphate supplements played significant role in maintaining phosphate level up to definite level in body and showed 100 % success to treat Hypophosphatemia in HD patients. Hyperphosphatemia occurred in 90% of HD patients that resulted in tetany and muscle tauting which was treated by avoiding Phosphate rich diet and Phosphate supplements. Vit D supplements were also prohibited in hyperphosphatemia patients. Medications to control hyperphosphatemia included diuretics which were used by 90% of HD patients. Renavel which is a phosphate binder was also used by 66% of HD patients. In HD patients Hemoglobin (Hb) level was maintained by Epokine or Venofer injection in 30% , Iron supplements in 58%, Vit B12 supplements in 12 % patients.

In our study, uremic fetor and xerostomia were reported in 63.63% and 72.72% patients respectively and these were consistent with results of Ahmed, et al., 2015 as they reported uremic fetor 66.1% & dry mouth 76.1%. Unpleasant taste was reported in 60.60 % patients of our study while Ahmed et al., 2015 reported it in 64.2% patients. The exact mechanisms behind the altered taste sensation in uremia patients are not established yet, but probable cause is the effect of ureamic toxins on the central and the peripheral nervous system controlling the taste receptors (Oyetola et al., 2015).

Gingival hyperplasia and associated bleeding gum issue was seen among 15.15 % patients which is lesser than 33.9% prevalence as reported by Ahmed, et al., 2015. Khan, et al., 2018 reported bleeding gum and gingivitis among 26% CKD subjects. Oyetola et al. BMC Oral Health (2015) 15:24]

Oral candidiasis was seen more commonly in CKD patients and it might be associated with immune suppression because of malnutrition, restricted diet, anemia and stress (Kuravatti, et al., 2016). In our study, we found burning sensation 51.51%, dry fissure lips 27.27%, candidiasis 9% & angular cheilitis in 36.36% cases while Ahmed et al., 2015 reproted burning sensation in 25.7%, dry fissure lips in 20.2%, candidiasis in 8.3% & angular cheilitis in 9.2% cases.

CONCLUSION

Chronic kidney disease has become a major concern in public health worldwide and number of patients needing a kidney transplant is increasing. The oral rehabilitation of renal patients is complexed by systemic effects of renal failure, specially; anemia, bleeding problems, cardiovascular diseases or endocrine disturbances. Dental management can be performed by following a treatment protocol designed after discussing and coordinating with the nephrologist. Patients should be treated by keeping in view all systemic effects correlated to kidney dysfunction and scheduled follow-up should be

maintained. Early diagnosis of oral and dental pathologies, good prophylaxis and patient education have central role in management.

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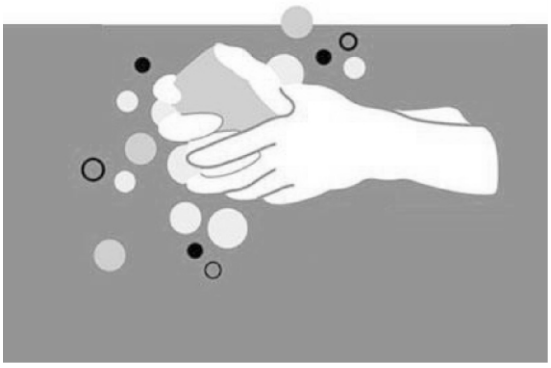

EXPERIENCE OF TREATING INFECTED WOUNDS WITH HYDROGEN PEROXIDE

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Abstract

Objectives: Since ancient times different pharmacological items are being tried for treatment of wound sepsis and non-healing. Multiple factors are involved in the process of healing. Our aim of the study was to show effects of hydrogen peroxide dressings for the treatment of infected wounds as compared to other modalities of treatment.

Methods: This prospective study was conducted at Avicenna Medical College & Hospital from September 2018 to December 2018. Thirty patients were randomly added in the study. Inclusion criteria was all types of infected wounds & exclusion criteria was clean incised wounds.

Results: We successfully treated many septic wounds and saved limbs by this technique which had been planned for amputations.

Conclusion: Hydrogen per oxide soaked dressings is a better modality for treatment for infected wounds as compared to other treatment modalities used till now.

Key Words: Infected wounds, Wound healing, Hydrogen peroxide

Management of traumatic and surgical wounds has had a chequered history. For example, in 1346 at the Battle of Crécy, France, foot soldiers were issued with cobwebs to staunch haemorrhage caused by trauma. Two centuries later, the eminent surgeon Ambroise Paré (1510-1590) rejected boiling oil as a primary dressing after amputation, preferring a mixture of oil of turpentine, rose-water, and egg.[1] The emergency department is frequently the presenting location for acute wounds, which is appropriate given its convenience, resources, and expertise. Acute wounds are often precipitated by trauma, such as burns, lacerations, or abrasions.[2]

Without proper cleansing and wound care, these acute wounds can lead to complications, such as poor healing and infection. Optimizing wound healing through proper acute wound management involves removal of harmful debris/necrotic tissue, exploration for underlying injuries, control of bacterial burden and appropriate closure. A comprehensive evidence-based approach to acute wound management is an essential skill-set for any emergency department physician or acute care practitioner. As the historical and clinical features surrounding the cutaneous injury process differ, wounds must be evaluated and treated individually.[3]

The risk of infection in traumatic wounds is reduced by adequate wound cleansing and debridement with removal of any non-viable tissue and foreign material. If severe contamination is present, broad spectrum antibiotic prophylaxis is indicated and should be extended as specific therapy as recommended for surgical wounds that are classed as "dirty" or when there are early signs of infection. Traumatic wounds need tetanus prophylaxis (parenteral benzyl penicillin and tetanus toxoid, depending on immune status). Strong evidence supports the use

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of antibiotic prophylaxis and treatment for surgical wounds that are classed as "clean contaminated" or "contaminated." The value of antibiotic prophylaxis in "clean" wounds is controversial but is widely accepted in prosthetic surgery (such as hip and knee replacement and synthetic vascular bypass surgery).[4]

Wound healing occurs primarily in three phases – inflammation, migration and remodeling. The successful wound healing is facilitated by plate-lets, fibroblasts, and keratinocytes. Most chronic wounds are related to diabetes mellitus, venous stasis, peripheral vascular diseases and pressure ulcerations. An open wound is favored by bacteria for biofilm formation and colonization. Biofilms make phagocytosis difficult, increase resistance to antibiotics and adhere to chronic wounds.

Primary closure, also known as healing by first intention, represents closure of a wound at the time of initial presentation. Wound edges are approximated with suture, adhesives, staples, or strips after appropriate wound management techniques are applied. Delayed primary closure represents a delay in wound closure for approximately 3–5 days. This is ideal for delayed presentations or for wound infection concerns. If there are no signs of infection and the wound margins appear healthy, removal of devitalized tissue and subsequent primary closure is appropriate.Healing by secondary intention represents those wounds that are allowed to heal through contraction—a natural, unaided physiologic property. While appropriate wound management practices are involved, no attempt is made to aid wound closure.[3]

The measures that have been recommended to reduce SSI include supplemental oxygen use[6,7] no bowel preparation in elective bowel resection,[8] preoperative skin antisepsis,[9] perioperative normothermia,[10] intravenous fluid restriction,[11] antimicrobial-impregnated sutures,[12] wound edge protection devices and tight glycemic control.[4]

Dressing is designed to be in contact with the wound, which is different from a bandage that holds the dressing in place. Historically, wet-to-dry dressings have been used extensively for wounds requiring debridement. In 1600 BC, Linen strips soaked in oil or grease covered with plasters was used to occlude wounds. Clay tablets were used for the treatment of wounds by Mesopotamian origin from about 2500 BCE. They cleaned wounds with water or milk prior to dressing with honey or resin. Wine or vinegar usage for cleaning the wounds with honey, oil and wine as further treatment was followed by Hippocrates of ancient Greece in 460- 370 BCE. They used wool boiled in water or wine as a bandage.[10]

There was a major breakthrough in the antiseptic technique during the 19th century, antibiotics were introduced to control infections and decrease mortality. Modern wound dressing arrival was in 20th century.[13,14] "Woven absorbent cotton gauze was used in 1891. Until the mid-1900's, it was firmly believed that wounds healed more quickly if kept dry and uncovered whereas 'closed wounds heal more quickly than open wound' written in an Egyptian medical text -Edwin smith surgical papyrus in 1615 BC. Oscar Gilje in 1948 describes moist chamber effect for healing ulcers. In the mid 1980's, the first modern wound dressing were introduced which delivered important characteristics providing moisture and absorbing fluids (e.g. polyurethane foams, hydrocolloids, iodine-containing gels). During the mid-1990's, synthetic wound dressings expanded into various group of products which includes hydrogels, hydrocolloids, alginates, synthetic foam dressing, silicone meshes, tissue adhesives, vapor-permeable adhesive films and silver/collagen containing dressing.

Currently more than 3000 types of dressings are available in the market making the physician to address all aspects of wound care. But still there is no superior product that heals chronic wounds like venous leg ulcers, diabetic wound and pressure ulcers which often fail to achieve complete healing. Hence developing a dressing material that addresses the major interfering factors of normal healing process will help patients and wound care practitioners largely.[15] Vacuum-assisted techniques to assist early wound closure have gained popularity in both civilian and military patients through their ability to facilitate early fascial closure in the presence of complex and contaminated wounds.[4,16,17]

Hydrogen peroxide has been used in medicine for more than 100 years. It is known in surgery as a highly useful irrigation solution by virtue of both its hemostatic and its antimicrobial effects[18] Hydro-gen peroxide (H_2O_2) is a topical antiseptic used in wound cleaning which kills pathogens through oxidation burst and local oxygen production. A proper level of H_2O_2 is considered an important requirement for normal wound healing. Wound healing is a tightly controlled process in which H_2O_2 plays multiple functions. Apart from killing micro-organisms, H_2O_2 also serves as a signaling molecule or second messenger which delivers a damage message and stimulates effector cells to respond.[19,20]

Reactive Oxygen Species, developed by the immune system, lead to the generation of hydrogen peroxide. The activated myeloperoxidase converts the hydrogen peroxide to hypochlorous acid (HOCl), which is highly active against all bacterial, viral, and fungal human pathogens.[3] The biological effect of H_2O_2 is dose dependent during the wound-healing process. For example, in relatively high concentrations, H_2O_2 displays its strong ability of oxidization and proinflammation to disinfect wound tissue; however, in comparatively low con-centrations, H_2O_2 assists in removing cell and pathogen debris and promotes secretion of cytokines which help tissue regeneration.[21,22,23] H_2O_2 is also used regularly to prepare the bony bed in cemented arthroplasties as well as to achieve hemostasis in neurosurgery.[24,25] It is also an adjunct hemostatic to topical epinephrine in patients with known platelet dysfunction after burn excision.[26] Equally impor-tant, it has an inherent risk of fatal oxygen embolism formation[27,28]

METHODOLOGY

This prospective study was performed at Avicenna Medical College & Hospital from September 2018 to December 2018. Thirty patients were included in this study randomly. Inclusion criteria was all types of infected wounds & incised clean wounds were excluded from the study.

RESULTS

Thirty patients with infected wounds on different parts of the body were included in the study (Table 1)

All wounds were washed with normal saline first & then hydrogen peroxide soaked gauze pieces were packed in the wounds. The outcome was better than all previous treatments which these patients tried before this modality.

Their duration of stay in the hospital & follow-up was also reduced & they showed higher level of satisfaction than previous modalities they tried.

DISCUSSION

A 3% solution of hydrogen peroxide is a commonly used wound antiseptic.[28] However; few studies report on its efficacy in wound healing and as an antiseptic, and its use remains controversial. While some studies have shown hydrogen per-oxide to be cytotoxic to healthy cells and granulating tissues, other animal, and human studies have shown no negative effect on wound healing.[29,30] Several studies have also shown hydrogen peroxide to be ineffective in reducing bacterial count.[31] The Ameri-can Medical Association summarized that the effer-vescing cleansing action of hydrogen peroxide might act as a chemical debriding agent to help lift debris and necrotic tissue from the wound surface when used at full strength.[32] Irrigation with normal saline after full-strength hydrogenperoxide use is recommended. Hydrogen peroxide was first used as a disin-fectant by an English physician in 1858 and was marketed under the name Sanitas. The 3% solution was popular for use on wounds from about 1920 to 1950. Hydrogen peroxide kills bacteria by de-composing to hydroxy radicals. It is produced by living cells to protect the body from harm caused by bacteria.[32] A study with Escherichia coli exposed to a constantly replenished stream of hydrogen per-oxide showed that bacterial growth was inhibited by 0.02-0.05 mmol/l hydrogen peroxide, a concent-ration that was not damaging to fibroblast cells from human skin.[33] In our study, we observed in all 50 patients that when H_2O_2 was applied to fresh wounds, brownish bubbles resulted, then gradually fade to whitish day by day, and after 2 weeks, bubbling stopped, and the solution was clear and colorless during 2 minutes, we attributed that as a sign of the degree of the wound cleanness, or fading of infectivity. When hydrogen per-oxide solution is used for the dressing of gaped wounds, there lease of nascent oxygen from hydrogen peroxide oxidizes the debris, and the effervescence pushes it from the depth of the wound[(34)]. We also observed that the appearance of healthy granulation tissue was faster in the H_2O_2 patients than the normal saline patients, and might positively contribute to the faster and shorter healing time in the H_2O_2 patients. It takes around one week for hydrogen peroxide to prepare a healthy wound bed[(34)]. Despite the reputation that H_2O_2 might lead to the formation of the bad scar when used for wound dressing, our study showed no adverse effect at all. All wounds treated by H_2O_2 healed nicely without scarring. No local or systemic adverse effects of H_2O_2 use or signs of toxicity were observed or reported by any patient in our study. Although in our adopted postoperative practice, we recommend dressing once per day. Given the results of our study, we believe that a more detailed scienti-fic prospective studies should investigate the role of hydrogen peroxide in infected wounds, especially in communities were wound infection is a major occu-rrence

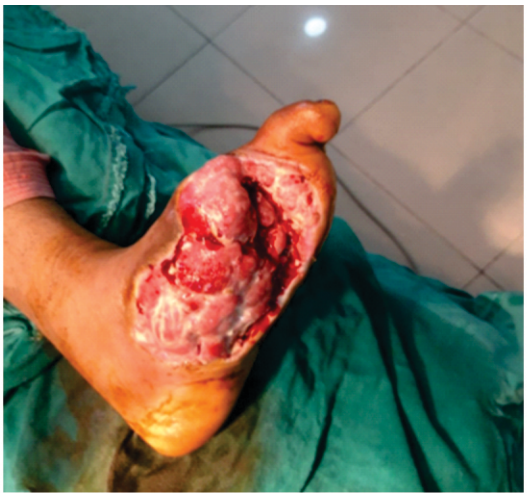
CONCLUSION

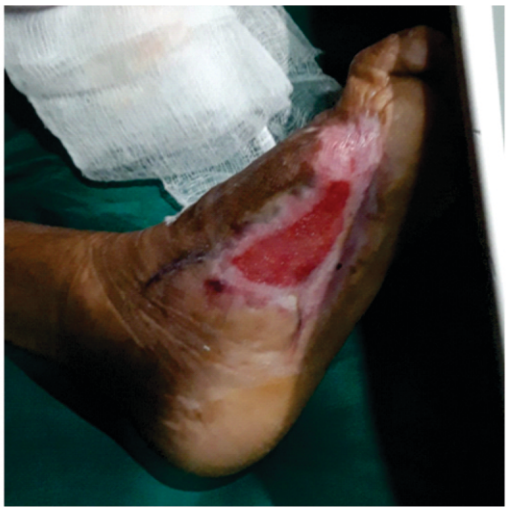
In the management of infected and septic wounds different pharmacological agents are used including pyodine, antibiotic sparys, antiseptic pow-ders, honey, vinegar and normal saline. Sometimes

Table 1: *Frequency of Allergies in a Sample of 300 Medical Students in Lahore, Pakistan, in 2014*

REGION	NO OF PATIENTS	PERCENTAGE
Upper limb	6	20
Lower limb	13	43.33
Torso	4	13.3
Perineum	7	23.3
TOTAL	30	100

you need culture sensitivities for appropriate drug and at other times limbs have to be amputated to manage the infected and septic wounds. But there is always some level of unsatisfaction with everything. Treated such wounds with H_2O_2 has shown very good results and we have saved some very dirty and





hopeless limbs. Also we have noted that it promotes healing at every level of wound healing.

LIMITATIONS OF STUDY

This study has some limitations.

1- This was not a double blind study.

2- Antibiotic prophylaxis and treatment were considered together during analysis which may have altered results of final outcome.

3- Misinterpretation of meaning in the written documentation is also a possible source of error.

4- Independent variables such as environmental conditions and socioeconomic status cannot be "controlled", may not even be "identified", and may "affect" the results.

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ROLE OF VITAMIN E IN PRIMARY DYSMENORRHEA

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Abstract
Introduction: Primary dysmenorrhea is defined as pelvic pain around the time of menstruation in the absence of an identifiable pathologic lesion, present from menarche. The pain is believed to be related to prostaglandin (PG). Vitamin E inhibits the release of arachidonic acid and the conversion of arachidonic acid to PG via an action on the enzymes phospholipase A2 and cyclooxygenase.
Objectives: To assess the decrease in mean pain score with vitamin E for management of females presenting with primary dysmenorrhea.
Study Design: Quasi experimental trial
Setting: Department of Obstetrics and Gynaecology, Unit-3 Jinnah Hospital Lahore.
Duration of Study with Dates: Study was carried out over a period of six months from 17-01-2017 to 16-07-2017.
Methods: Females were evaluated for menstruation pain at baseline by using VAS and pain score was noted. Then females were given vitamin E tablets. After 3 cycles females were re-assessed for pain score by using VAS.
Results: Patients ranged between 12-19 years of age. Mean age of the patients was 15.4±1.9 years. Mean BMI was 21.6±3.7 (Kg/m2), mean duration of menarche was 2.7±1.6 years. Majority of the patients were educated upto primary i.e. 62 patients (40%), followed by those educated upto middle school, 40 patients (25.8%), those upto matric 24 patients (15.5%) whereas 29 patients (18.7%) were illiterate. Mean pain score at baseline was 7.63±1.17 and mean pain after 3 cycles was 3.67±1.48 ($p<0.001$). Stratification with regard to age, BMI, duration of menarche and educational status was also carried out.
Conclusion: In conclusion, vitamin E administration in women, who suffer from primary dysmenorrhea, significantly reduces the pain. It can be used as an alternative treatment method in affected women.
Key Words: Primary dysmenorrhea, Pain, Vitamin E

Dysmenorrhea is defined as a cyclical cramping pain occurring just before or during menstruation that adversely affect the daily activities of the females.[1] Primary dysmenorrhea is one of the most common menstrual complaint. It is frequently self-treated by patients of all ages. Teenagers are especially prone to experiencing dysmenorrhea symptoms and selecting over the counter therapies without adult supervision.[2]

Dysmenorrhea is the most common menstrual complaint in the United States, impacting more than 50% of women over the course of their lifetime. Primary dysmenorrhea is specifically defined as recurrent, crampy abdominal pain that occurs in the absence of any abnormal pelvic pathology.[3]

Several treatments have been suggested for dysmenorrhea, such as using prostaglandin inhibiting drugs, non-steroid anti-inflammatory drugs, oral contraceptive pills, vitamins, herbal substances, etc. The most frequent side effects brought about by drugs controlling prostaglandins are mild digestive disorders such as nausea, indigestion, vomiting and epigastric pain. These treatments in addition to their curative effects present with undesirable side effects which makes them tedious to use. Various studies have pointed out the effect of vitamins such as E and B on menstrual pains. The antioxidant quality of vitamin E can prevent the formation of prostaglandins which decreases dysmenorrhea.[4]

One study reported that with vitamin E, pain score was reduced from 6±0.75 to 0.5±0.[5] after three cycles and mean decrease of 5.5±0.25 pain was noted.[5] Another study also reported that with vitamin E, pain score was reduced from 55.7742 to 45.1398

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after three cycles and mean decrease of 10.6344 pain was noted which was less than that reported in the above study.[6]

The purpose of this study was to assess the decrease in mean pain score with vitamin E for management of females presenting with primary dysmenorrhea. In routine practice, females take NSAIDs for dysmenorrhea by themselves or are recommended by the physicians. In the developing countries like Pakistan, the nutritional health is poor especially of females. This cause deficiency of important nutrients from body including vitamins which are main cause of dysmenorrhea. Addition of vitamin E supplementation can aid in reducing dysmenorrhic pain in menstruating girls. But very little evidence is available in this regard and furthermore, no local study was found in literature. We conducted this study to get the local evidence so that in the future, we can plan therapeutic programs for better health and to reduce dysmenorrhea. This will improve our practice in dealing with this menstrual problem. Also, through this study we will be able to assess the local magnitude of the disease.

Vitamin E

Vitamin E was discovered for the first time in 1992 during a research on the relationship between nutrition and fertility by Evans and Bishop. As it was revealed that this vitamin inhibits arachidonic acid release and its conversion to prostaglandin. It could also increase internal opioids thus causing pain relief.[7]

Vitamin E inhibits the release of arachidonic acid and the conversion of arachidonic acid to PG via an action on the enzymes phospholipase A2 and cyclooxygenase.[8] The treatment with 500 IU vitamin E therapy daily significantly reduced the severity of pain in primary dysmenorrhea[9] Vitamin E is available commercially as a chewable tablet containing 100 IU and a liquid capsule containing 200 IU. The present study was designed to study the effect of a lower dose of 400 IU vitamin E on pain and menstrual blood loss in the treatment of primary dysmenorrhea. The duration of treatment was extended to four months.

OBJECTIVES

- To assess the decrease in mean pain score with vitamin E for management of females presen-ting with primary dysmenorrhea.

OPERATIONAL DEFINITIONS

Primary Dysmenorrhea: It was defined as lower abdominal pain occurring during menstrual cycle by using visual analogue scale (VAS) score >5. Pain should be present for at least 3 consecutive preceding cycles and there should be no underlying pathology causing the disease.

Decrease in Pain Score: It was measured as difference between baseline and after treatment pain score through subtraction of after treatment pain score from baseline pain score. Treatment was given for 3 cycles and after 3 cycles, pain was measured at 4th month.

METHODOLOGY

STUDY DESIGN

Quasi experimental trial

SETTING

Department of Obstetrics and Gynaecology, Unit-3 Jinnah Hospital Lahore.

DURATION OF STUDY WITH DATES

Study was carried out over a period of six months from 17-01-2017 to 16-07-2017.

SAMPLE SIZE

Sample size of 155 cases was calculated with 95% confidence interval d=0.08 and taking magnitude of decrease in mean pain score i.e. 5.5±0.25 with vitamin E for management of primary dysmenorrhea.[5]

SAMPLING TECHNIQUE

Non-probability, consecutive sampling

SAMPLE SELECTION

Inclusion Criteria

Girls of age 12-19 years presenting with primary dysmenorrhea (as per operational definition).

Exclusion Criteria

- Married females

- Females with primary or secondary infertility (on medical record).
- Females with polycystic ovarian syndrome (on USG) polycystic ovaries and evidence of hirsutism.
- Females with chronic systemic problems like hypertension (BP>140/90mmHg), diabetes (BSR>186mg/d1,), anemia (Hb<10mg/d1).

DATA COLLECTION PROCEDURE

155 females fulfilling selection criteria were enrolled in study from OPD of Department of Obstetrics & Gynecology, Jinnah hospital, Lahore. Informed consent was obtained. Demographic information (name, age, BMI, duration of menarche) was obtained. Then females were evaluated for menstruation pain at baseline by using VAS and pain score was noted. Then females were given vitamin E. Vitamin E packages contain 10 Capsules, each containing 200 units of vitamin E. Each female was advised to take one capsule twice daily for five days (two days before and three days after the beginning of menstruation), for 3 consecutive cycles. Then females were followed up in OPD for three cycles. After 3 cycles females were re-assessed for pain score by using VAS. Decrease in pain score was measured (as per operational definition) All this information collected through a pre-designed proforma (attached).

DATA ANALYSIS PROCEDURE

Data were entered and analyzed by SPSS version 20. Quantitative variables like age, BMI, duration of menarche, pain score at baseline and after treatment was calculated as mean and standard deviation. Difference between baseline and after treatment pain score was calculated through subtraction of after treatment pain score from baseline pain score. Paired-sample t-test was applied to assess the significance of decrease in mean pain score. P value ≤ 0.05 was taken as significant. Data was stratified for age, BMI and duration of menarche and educational status. Paired-sample t-test was applied taking p value ≤0.05 as significant.

RESULTS

A total of 155 patients were including in the study during the study period of six months from 17-01-2017 to 16-07-2017.

Patients ranged between 12-19 years of age. Mean age of the patients was 15.4±1.9 years. Mean BMI was 21.6±3.7 (Kg/m^2), mean duration of menarche was 2.7±1.6 years. Majority of the patients were educated upto primary, 62 patients (40%), upto middle school, 40 patients (25.8%), upto matric 24 patients (15.5%) and rest were illiterate, 29 patients (18.7%). Mean pain score at baseline was 7.63±1.17 and mean pain after 3 cycles was 3.67±1.48 ($p< 0.001$). Stratification with regard to age, BMI, duration of menarche and educational status was also carried out.

DISCUSSION

Dysmenorrhea occurs in 40% of adult menstruating women and over 10% report severe limitation of social activity for one to three days per cycle[10] leading to the socio-economic burden of such limitations. Primary dysmenorrhea occurs as a

Table 1: Distribution of Patients by Age

Age (Year)	Number	Percentage
12-16	109	70.3
17-19	46	29.7
Total	**155**	**100.0**
Mean±SD	**15.4±1.9**	

Table 2: Distribution of Patients by BMI

BMI (kg/m ^{2})	Number	Percentage
≥ 25	130	83.9
≥ 25	25	16.1
Total	**155**	**100.0**
Mean ± SD	**21.6 ± 3.7**	

Table 3: Duration of Menarche

Duration (year)	Number	Percentage
1-4	129	83.2
5-7	26	16.8
Total	**155**	**100.0**
Mean ± SD	**2.7±1.6**	

Table 4: Educational Status

Education	Number	Percentage
Illiterate	29	18.7
Primary	62	40.0
Middle	40	25.8
Matric	24	15.5
Total	**155**	**100.0**

Table 5: Comparison of Mean Pain Score for Management of Primary Dysmenorrhea with Vitamin E

Group	Mean	Standard deviation
Pain at baseline	7.63	1.17
Pain after 3 cycles	3.67	1.48
t value	33.400	
p value	**P < 0.001**	

Table 6: Stratification for Age with Regard to Mean Pain Score

Age (Year)	Group	Mean pain score		P value
		Mean	S.D	
12-16	Pain at baseline	7.75	1.23	P<0.001
	Pain after 3 cycles	3.84	1.49	
17-19	Pain at baseline	7.35	0.99	P<0.001
	Pain after 3 cycles	3.26	1.40	

Table 7: Stratification for BMI with Regard to Mean Pain Score

BMI (kg/m^2)	Group	Mean pain score		P value
		Mean	S.D	
≤ 25	Pain at baseline	7.62	1.22	P<0.001
	Pain after 3 cycles	3.66	1.46	
≥ 25.1	Pain at baseline	7.68	0.94	P<0.001
	Pain after 3 cycles	3.72	1.64	

Table 8: Stratification for Duration of Menarche with Regard to Mean Pain Score

Duration (Year)	Group	Mean pain score		P value
		Mean	S.D	
1-4	Pain at baseline	7.69	1.23	P<0.001
	Pain after 3 cycles	3.80	1.50	
5-7	Pain at baseline	7.35	0.84	P<0.001
	Pain after 3 cycles	3.04	1.21	

Table 9: Stratification for Educational Status with Regard to Mean Pain Score

Educational status	Group	Mean pain score		P value
		Mean	S.D	
Illiterate	Pain at baseline	7.48	1.09	P<0.001
	Pain after 3 cycles	3.14	1.12	
Primary	Pain at baseline	7.60	1.22	P<0.001
	Pain after 3 cycles	3.71	1.56	
Middle	Pain at baseline	7.90	1.15	P<0.001
	Pain after 3 cycles	3.88	1.53	
Matric	Pain at baseline	7.46	1.21	P<0.001
	Pain after 3 cycles	3.88	1.51	

result of PG-induced myometrial contractions. The PGs also contribute to uterine ischemia, and sensitization of afferent nerve fibres to painful stimuli. NSAIDs are an effective treatment but are contraindicated in some women, and only moderately effective in others. The combined contraceptive pill (COC) suppresses the progesterone-driven proliferation of the secretory endometrium during the luteal phase, thus resulting in a decrease in PG synthesis and the volume of menstrual fluid. The COC is an accepted treatment for dysmenorrhea in non-adolescent women, but the efficacy of low dose COC pill in the treatment of adolescent dysmenorrhea has yet to be determined[11]. Furthermore, prescribing the high dose COC pill from an early age may carry possible long-term risks. The use of vitamin E for dysmenorrhea in adolescent women is attractive because of the marked effect we have demonstrated coupled with the absence of significant side effects from vitamin E in therapeutic doses.

Vitamin E reduced the severity and the duration of pain from primary dysmenorrhea and also reduced the amount of menstrual blood loss. All of these effects can be attributed to the reduction of PG synthesis by vitamin E acting as an antioxidant and anti-Prostaglandin.

Primary dysmenorrhea is thought to be related to prostaglandin production, which is associated with pain. As such, vitamin E, which inhibits the release of arachidonic acid and its conversion to prostaglandin, represents a potential therapy. Indeed, previous research has shown that taking 500 IU vitamin E daily significantly reduces pain severity[9]. These findings are comparable with our results.

Vitamin E, composed of four tocopherol and tocotrienol components, is known to have antioxidant activity. α-tocopherol has antioxidant properties that can prevent chronic disease associated with oxidative stress[12]. Two Iranian studies reported vitamin E to be effective in reducing symptoms and degree of pain caused by dysmenorrhea. In addition, they reported that vitamin E caused a reduction in pain duration.[5,9] Similarly, current study demons-

trated that vitamin E reduced the duration of pain in primary dysmenorrhea.

CONCLUSION

In conclusion, vitamin E administration in women, who suffer from primary dysmenorrhea, significantly reduces the pain. It can be used as an alternative treatment method in affected women.

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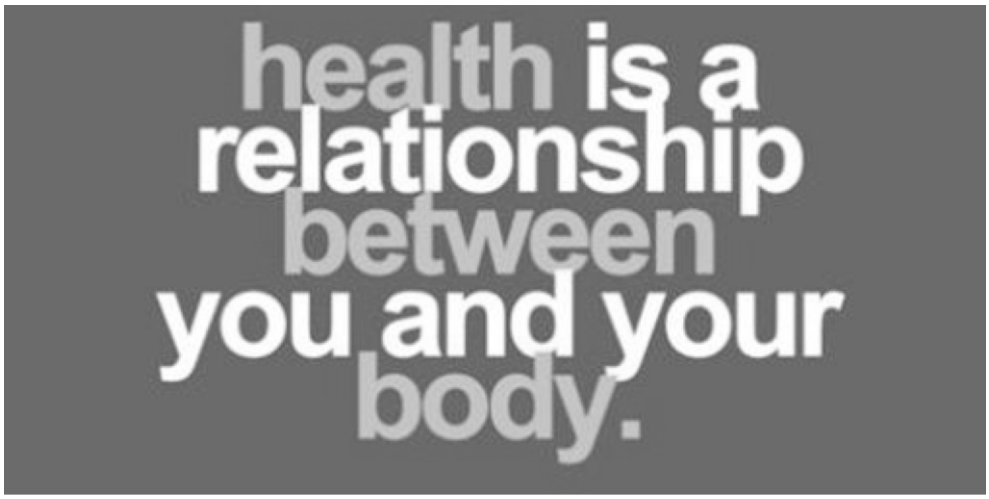

FOOT FILLET FLAP: A DURABLE AND SENSATE OPTION FOR THROUGH AND BELOW KNEE AMPUTATIONS

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Abstract

Background: Foot fillet flap can be utilized to cover the through and below knee amputation stumps as an alternative to local skin flaps. Although a lucrative option, it is rarely available as uninvolved sole of foot with intact innervation is required for execution. We present a case series to describe its durability and sensation to characterize its utility, which are not published before in the literature.

Methods: This descriptive case series was done at Jinnah burn and reconstructive surgery center Lahore. Patients who had either through and below knee amputation with one year follow up, operated between January 2015 to December 2018 were included in the study. Patients were followed in out patient department and assessment was done regarding scar problems, ulceration, wound breakdown, soft tissue infection, fine touch and two point discrimination (2 PD).

Results: 9 patients were included in the study, majority of whom were post traumatic. The average pre-op fine touch was 9.1 ± 0.6 as compared to 8.2 ± 0.4 post operatively (p=0.71). One patient presented with hyperalgesia at the surgical site. Mean static 2 PD of the flaps were 30.3 ± 2.3 mm as compared to 20.6 ± 1.9mm of the contralateral feet (p=0.12). The mean dynamic 2 PD of the flaps were 25.3 ± 3.3 as compared to 21.0 ± 1.8mm of contralateral uninvolved feet (p=0.43).

Conclusion: Foot fillet flap offers a durable and sensate coverage option for through and below knee amputations.

Key words: Foot Fillet Flap, Below Knee Amputation

Salvage of lower extremity is often not possible in cases of mangled extremity, extensive tumors, osteomyelitis etc.[1] Coverage of the stump with sturdy tissue is required as the stump has to bear extensive shear and pressure when prosthesis is applied.[2, 3] Either dorsoventeral or lateral flaps can be used to cover the stump, but are often not durable and have less proprioception as compared to the original weight bearing surface, i.e the plantar surface of foot.[4] Spare part surgery is one of the techniques used in plastic surgery, utilizing the viable tissues for reconstruction rather than discarding them. Utilizing foot fillet flap is one of such techniques where the islanded skin flap of foot is used as part of the spare parts surgery.[5] It is suitable when lower extremity amputation Is planned and foot is relatively spared with intact sensation and vascularity.[6] Although studies utilizing the fillet flap have been published, but none have described its durability, in terms of long term stable coverage and fine sensation and proprioception, which is necessary for better ambulation when prosthesis is used. We present case series

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of utilizing islanded pedicled foot fillet flap to cover through and below knee amputations, describing its durability in terms of wound breakdown and sensation to further characterize its utility.

METHODOLOGY

This descriptive case series was done in Jinnah burn and reconstructive surgery center Lahore. After approval from ethical review board, We included 9 patients of either gender, who underwent through or below knee amputation due to any etiology between January 2015 to December 2019 at our center, and in whom pedicled islanded foot fillet flap was used with at least 1 year of follow-up period. We excluded patients who had any co-morbidity effecting sensation of the lower limb, neuropathy and those with bilateral lower limb amputations. Patients were requested to come in out patient clinic and assessment was done regarding scar problems, ulceration, wound breakdown, soft tissue infection and sensation. Fine touch over the flap covering the stump was assessed and compared to the contralateral uninvolved plantar surface of foot on a scale of ten and to the pre-operative findings from the record. If it was less than 10/10, then 2 point discrimination was done comparing it to the contralateral foot. To minimize the bias, the first author examined all the patients and checked the fine sensation with cotton swab. Two point discrimination was checked with Castroviejo calipers, with a maximum scale of 40mm. Data was recorded and then analysis was done. Figure 1 shows a female patient who underwent through knee amputation due to post traumatic knee joint ankylosis and loss of function of common peroneal nerve. Pedicled foot fillet flap was done based on posterior tibial vessels and tibial nerve together with the branches was retained to provide sensation. The neurovascular bundle was tucked under the flap during the inset.

RESULTS

Majority of the patients were male i.e. 6(66.7 %), while there were 3 female patients (33.3%). 7 patients had undergone below knee amputation while 2 underwent through knee amputation. 7 Patients presented either immediately acutely after trauma with unslavagabe limb necessitating amputation or due to sequel of trauma to lower limb with no possibility of reconstruction to make the limb usable. None of the patients experienced ulceration, infection or hypertrophic / keloid scar. 1 patient had wound breakdown after use of prosthesis which resolved after use of conservative measures for wound healing and adjusting the fitting part of prosthesis. Only two patients had comparable sensations over the sole of foot. The average pre-op fine touch was 9.1 ± 0.6 as compared to 8.2 ± 0.4 post operatively (p=0.71). One patient presented with hyperalgesia at the surgical site. Mean static 2 PD of the flaps were 30.3 ± 2.3 mm as compared to 20.6 ± 1.9mm of the contralateral feet (p=0.12). The mean dynamic 2 PD of the flaps were 25.3 ± 3.3 as compared to 21.0 ± 1.8mm of contralateral uninvolved feet (p=0.43). Table 1 summarizes finding of the study.

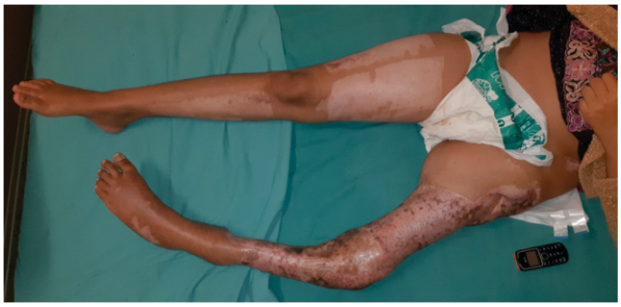

Table 1:

Gender	Level of amputation	Etiology	Fine touch Pre-Op out of 10	Fine touch post op out of 10	Static 2PD (mm). Flap / Normal foot	Dynamic 2PD (mm). Flap / Normal foot	Pain/phantom limb sensation/ hyperalgesia	Using prosthesis
Male	Below Knee	Post Traumatic	9	8	32/27	24/21	No	Yes
Female	Through Knee	Post Traumatic	9	9	30/28	21/20	No	Yes
Male	Below Knee	Malignancy	10	8	31/30	26/24	No	Yes
Male	Below Knee	Post Traumatic	9	8	35/25	32/22	No	No
Female	Below Knee	Post Traumatic	9	8	29/24	27/23	No	Yes
Male	Below knee	Malignancy	10	9	28/27	23/21	No	Yes
Male	Through Knee	Post Traumatic	9	8	31/25	27/20	Yes	Yes
Male	Below Knee	Post Traumatic	9	8	30/26	26/20	No	Yes
Female	Below Knee	Post Traumatic	9	8	27/25	22/18	No	No

DISCUSSION

Foot fillet flap is an indispensable tool to cover the stump after lower limb amputations as it offers coverage with like tissue which is durable and can bear shearing forces.[7] Although improvement in design and fitting of prosthesis for lower limb results in excellent long term outcome with minimum stump revisions, availability of relatively spared sole of foot allows longer stumps without the need to go proximally to obtain stable coverage. Despite this, foot fillet flap is usually unavailable as most amputations are done in patients with diabetes and those suffering form any vascular disease. [8]

In cases where lower limb amputation was planned due to malignancy, neurovascular bundles were spared, that why pre operatively patients had full sensation over the sole of foot. On the contrary, patients with history of trauma had decreased sensation due to either direct trivial injury or fibrosis. Nevertheless patients had 80% more sense of fine touch after the procedure. This maybe due to the dissection around the neurovascular bundle and further fibrosis.

As sole of foot provides a sensate and sturdy tissue to absorb the stress and shearing forces over the stump, hence none of the case developed ulcers or infection due to wound breakdown. Only one patient developed breakdown at the suture site due to ill fitting prosthesis. His wounds healed after conservative measures and adjusting the prosthesis. Hence the islanded pedicled fillet flap provides a stable coverage for the stump as it adjusts the best tissue at the stump.

Two point discrimination of sole of foot ranges from 6mm to 27mm. However, the lowest distance is measured over the big toe and lesser over the other areas.[4,9] This also varies from individual to individual. So to minimize the bias, we measured and compared the 2 PD over roughly the similar areas of foot and the flap. The average difference of static 2PD was around 10mm and 5mm dynamic between foot fillet flap and normal foot, which was not significant. Various studies have stressed that the specific technique for measuring the 2 PD. It is traditionally measured with a rubber studded with pins at various distances and pinheads are used to measure the distance. The pinheads are fixed at specified distances, allowing measurements to be measured with a minimum distance of 2 – 3mm. We used caliper with a scale of 40mm to measure the distance as it allowed to measure the distance with a minimum difference of 1mm.

Phantom limb sensation, hyperalgesia and burning sensation is common when local flaps are used to cover the stump. This is attributed to division of the nerve and the neuroma at the ending cause the symptoms. When pedicled islanded foot fillet flap is used, the nerves are retained as such and the chances for all these symptoms are minimal.

CONCLUSION

Thus we conclude that pedicled foot fillet flap provides a sturdy coverage for through and below knee amputations. There are minimal chances of developing ulceration and wound complications with the use of this technique. The flap provides a sensate coverage and so provides a better long term option for stump reconstruction.

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HOW TO PREVENT POST LAPAROSCOPIC CHOLECYSTECTOMY CYSTIC DUCT REMNANT SYNDROME

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Abstract

Background: Since many years, laparoscopic cholecystectomy is the gold standard operation for symptomatic gallstones. The similar abdominal pain that primarily was the indication for surgery, can occur after this operation in 5-10% patients. This is defined as "post-cholecystectomy syndrome". Biliary disorders like residual choledocholithiasis, bile leak or stenosis, biliary dyskinesia&some non-biliary diseases can cause this syndrome. Cystic duct remnant syndrome is rare etiology for it.

To outline the Calot's triangle anatomy is very important during cholecystectomy, to avoid the iatrogenic injury to surrounding structures. The Hartman pouch of the gallbladder, is retracted laterally& inferiorly for this purpose. If the Hartman's pouch is pulled superiorly, the gallbladder stones can slip through cystic duct into the common bile duct. During clipping & cutting of the cystic duct if the stone slips & impacted in the cystic duct just proximal to its junction with the common bile duct, the cystic duct remnant syndrome develops.

Objectives: To prevent the cystic duct remnant syndrome after laparoscopic cholecystectomy with the help of meticulous dissection of Calot's triangle and lateral & downward retraction of the Hartman's pouch of the gallbladder.

Methods: Twenty cases of laparoscopic cholecystectomy were operated at Avicenna Medical & Dental College, Lahore from January 2019 to June 2019. All patients were prepared preoperatively with necessary investigations & anesthesia fitness. Three port & four port laparoscopic cholecystectomy was performed & no case was converted to open cholecystectomy. Post-operative proforma was filled & symptoms of cystic duct remnant syndrome were evaluated for diagnosis.

Results: One patient out of twenty was diagnosed and managed for cystic duct remnant syndrome

Conclusion: Patients can develop persistent symptoms after laparoscopic cholecystectomy when they retain stone in the cystic duct stump. These patients can be managed conservatively &operated only when not settled. Laparoscopic surgery is not a contra-indication for this revision surgery. During laparoscopic cholecystectomy, lateral & outward retraction of the Hartman pouch is safe & prevents the development of cystic duct stump syndrome

Key Words: Laparoscopic Cholecystectomy, Cystic Duct Stump Syndrome, Hartman's Pouch

Open surgery has been replaced by laparoscopic cholecystectomy for the treatment of symptomatic gallstones.[1–8] Except several advantages, the complication spectrum in the laparoscopic approach has been increased as compared to open procedure, particularly bile duct injury which raised

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from 0.3 to 0.6%.

After cholecystectomy, between 5 and 15% of patients can experience the episodes of abdominal pain similar to the pain that motivated them for surgery.[9,10] This is called "post-cholecystectomy syndrome". The etiology can vary, such as residual choledocholithiasis, bile leak or stenosis, biliary dyskinesia and some non-biliary diseases as well.[11,12] Cystic duct remnant syndrome is less frequent but important causing this post-operative pain.

The residual cystic duct greater than 1cm & calculi within its interior which can cause post-cholecystectomy syndrome is defined as cystic duct remnant syndrome.[13,14] Immediate postoperative period to even years after cholecystectomy can have this syndrome[9] causing the symptoms similar to biliary colic and even episode of cholestasis, as occurred in our case. It is a rare etiology of post-cholecystectomy syndrome. Due to the increasing number of laparoscopic cholecystectomies in recent decades, it is expected that it would become more frequent in future. [14,15]

Cystic duct remnant syndrome can be diagnosed by ultrasound, computed tomography and scintigraphy of the biliary system[11]. Magnetic resonance cholangio pancreatography (MRCP) is non-invasive choice for its evaluation.[10,13,16]

Other extra-biliary etiologies for post cholecystectomy syndrome, should also be ruled out such as irritable bowel syndrome, peptic ulcer & hepatitis.[11,17] Cystic duct remnant syndrome has been questioned as a cause of post-cholecystectomy syndrome, but when other causes have been excluded and imaging studies document a long cystic remnant with calculi[9] with no other findings, it should be considered as diagnosis. Cystic duct remnant syndrome can be associated with bile leak, biliary stenosis, biliary neuromas or granulomas.

Resection of the remnant is considered a definite treatment to resolve the symptoms in certain cases,[13,14,16] although redo-surgery is difficult due to fibrotic changes between the remnant and the main bile duct and has increased risk particularly in laparoscopic approach as compared with open surgery[10] Lithotripsy and ERCP are alternatives to the surgical treatment.[15]

Recurrent symptoms with demonstrated residual calculi in the cystic duct remnants is an indication for surgical intervention when other etiologies are excluded. Calculi in the cystic duct stump should be identified and managed during cholecystectomy either open or laparoscopic approach to prevent this syndrome[18] Secondly, proper dissection and anatomical identification of the union of the cystic duct with bile duct and lateral & downward traction of the Hartman pouch also prevents it.

METHODOLOGY

Twenty cases of laparoscopic cholecystectomy were performed at Avicenna Medical & Dental College, Lahore from January 2019 to June 2019. All patients were investigated for anesthesia fitness. Both three port & four port laparoscopic cholecystectomy were performed & none was converted to open cholecystectomy. Post-operative proforma was filled & cystic duct stump syndrome was diagnosed by analyzing the proforma

RESULTS

One out of twenty patients, was diagnosed as cystic duct remnant syndrome which was managed conservatively. She was operated for symptomatic gallstones. Her laparoscopic cholecystectomy was done. On 2nd post-operative day, she developed pain epigastrium which was severe, colicky & relieved mildly with pain killers. Ultrasound abdomen & LFTs were normal. MRCP showed impacted stone in cystic duct remnant, just below the cystic duct clips.

DISCUSSION

Cholecystectomy is the most common surgery for symptomatic gallstones and laparoscopic cholecystectomy is the "gold standard". Eighty five percent (85%) of patients get relief by this operation,[19] However in some patients, symptoms such as

pain and dyspepsia, may persist after surgery as post cholecystectomy syndrome.[20,21,22] This is due to residual stone in the gallbladder remnant because of partial cholecystectomy or in the particularly long cystic duct.[20,21,23] Its ratio seems to be slightly higher in laparoscopic cases than the ones with open cholecystectomy.[24,25] Poor visualization during laparoscopic surgery, Marked inflammation, dense adhesions in the acute phase of the disease, excessive bleeding, frozen porta hepatis and confounding gallbladder morphology are the reasons for incomplete resection of the gallbladder or division of the cystic duct close to the gallbladder to avoid iatrogenic common bile duct injury.[26,27]

However, some patients may suffer from upper abdominal pain similar to that they had before surgery. These symptoms that are known as post cholecystectomy syndrome may be due to biliary stricture, retained or recurrent biliary stone, "sphincter of oddi dysfunction" like stenosis or dyskinesia, remnant gallbladder or cystic duct stump stone.[22,26,28,29,30]

Patients at increased risk of stones in the cystic duct are those with history of recurrent biliary colics, pancreatitis, obstructive jaundice and those who underwent repeated intervention by ERCP before surgery.[31] To rule out the cause of this pain, ultrasonography, CT scan, ERCP, MRCP and EUS are used.[32,33,34] Ultrasound abdomen is often the first line investigation of such patient, but it can miss the diagnosis nearly in 50% of cases comparing to MRCP.[35]

In our report sonography reveald a cystic structure at gallbladder fossa with a stone inside it that suggested residual gallbladder or dilated cystic duct stump with remnant stone. Other non-invasive method is MRCP which needs no sedation and no radiation exposure risk. Moreover, its sensitivity and specificity is similar to those of EUS.[33] It has sensitivity between 85% to 100% in demonstrating biliary anatomy & stones.[35] In our case, MRCP also revealed the dilated cystic duct stump with remnant stone & determined the whole biliary tract anatomy.

To prevent the cystic duct remnant syndrome, proper dissection, identification of the gallbladder & cystic duct junction and lateral & downward traction of the Hartman pouch is a recognized methodology. Patients with a retained stone in the residual gallbladder or cystic duct remnant should undergo surgery if not settled with conservative approach. This surgery should be executed by a laparoscopic surgeon expert in such kind of re-do surgery.

This surgical intervention should be undertaken to resolve the symptoms and avoid potentially life-threatening complications such as carcinoma, recurrent cholangitis, mucocele formation, and Mirizzi syndrome.[30,36]

With the advances in laparoscopic surgery, modern instruments as well as increasing experty of surgeons, these cases can be operated laparoscopically. Previously open method was considered the "procedure of choice" for such kind of complicated re-do surgery. However, High surgical risk is a recognized fact in laparoscopic approach due to presence of inflammation and previous surgical adhesions.[19,37]

In 1995, Gurel et al. reported the first laparoscopic completion cholecystectomy.[38] Nowadays the laparoscopic approach on the biliary system appears to be a minimally invasive, safe and feasible when done by expert laparoscopic surgeons as a completion surgery, contrary to previous opinions.[39]

CONCLUSION

The cystic duct remnant syndrome can be prevented by "proper dissection and identification" of the gallbladder & cystic duct junction and "lateral & downward traction" of the Hartman pouch during laparoscopic cholecystectomy.

Patients with recurrent symptoms and established remnant duct stones should be operated if not settled with conservative approach and laparoscopic surgery is not a contra-indication for these revisional and re-do surgeries.

LIMITATIONS OF STUDY

This study has some limitations.

1- This was not a double blind study. American Society of Anesthesiologists classification were not included, while these criteria were used in most of the international studies. Antibiotic prophylaxis and treatment were considered together during analysis which may have altered results of final outcome.

2- A descriptive chart review may result in collecting "inaccurately charted information" from the medical record. Some charts had more thorough charting than others. Misinterpretation of meaning in the written documentation is also a possible source of error.

3- Extraneous variables such as environmental conditions and socioeconomic status cannot be "controlled", may not even be "identified", and may "affect" the results. Despite these limitations, this study provides valuable information regarding "successful revisional & re-do" management of post-cholecyctectomy cystic duct remnant syndrome by Laproscopic modality of intervention.

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ASSESSMENT OF COMMUNITY PERCEPTIONS AND PRACTICES REGARDING PREVENTION OF DENGUE FEVER

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Abstract

Objectives: To assess knowledge ,attitude and practices of health care seekers regarding dengue prevention and control.

Methodology: Cross sectional study. Study Area: Study has been conducted in government health care facilities of primary and secondary level in district Rawalpindi. Study Period: Study has been conducted during a period of 6 months from March 2019 to Sept 2019. Study Population: Community members visiting the health care facility for reasons other than dengue fever. Sampling Technique: Multistage sampling has been used to select the study participants . Source of Data: Primary source of data collection has been used. This data has been collected by face to face interviews with the help of a framed questionnaire. Sample Size: Was calculated using open epi software and came out to be 310. For facility based analysis, total of 31 facilities were recruited including 3 District level hospitals, all RHCs and THQs and 2 BHUs from each tehsil. 10 Community members from each facility were recruited and total community members from 31 facilities were 310.Result: All community participants recruited in the study (100%) knew about the disease but their core knowledge and practices were not good. Majority of them 76.1% know about the disease from their family, friends, neighbors or teachers. Those learn from doctors were 23.9%. Only 1 respondent shared that there is someone infected with the disease in his/her close vicinity that is his/her neighbor/friend and that person immediately contacted health facility for treatment. 41.3% respondents reported using bed nets while 58.7% people had not adopted that protection measure. 40.6% people among 128 participants revealed that they self purchased the bed nets. Only 2(0.6%) said that government provided these bed nets. Moreover, according to 41.3% people recruited in study, bed nets they used were not impregnated. The reasons for not using bed nets include un affordability (20.3%), hot weather (8.1%), and unpleasant smell (1.9%)

All Community members visited the health facility for the reason other than dengue, among them only 1% witnessed organization of awareness campaigns in their areas by government Health Team. They were also asked to provide some suggestions for dengue prevention and control. Majority (62.6%) suggested keeping environment clean and (9.7%) said to provide proper sanitation facilities,(16%) suggested for proper water drainage,(3.9%) suggested that there should be regular spray, (2.3%) gave importance to the use of bed nets, (0.6%) gave importance to the use of quil and lotion and (4.5%) suggested for the use of safe water.

Conclusion: The knowledge and attitude of the respondents concerning dengue control was not satisfactory, focusing more on the things which are not primarily concerned with dengue and they were giving less importance to the personal protective measures e.g the use of bed nets ,use of anti mosquito lotions ,use of quils, use of sprays which constitute cornerstone in dengue prevention and control.

Key words:- knowledge ,attitude, practice ,dengue, Rawalpindi

Dengue fever continues to be a potential public health threat in subtropical and tropical countries for the past decades where 2.5 billion population is at risk of getting disease.[1] It is the most significant challenge, world is facing since 1980s and has become a major public health concern globally with 70% occurrence rate in Asia Pacific alone.[1] In 2012 ranking, dengue fever considered as the most significant vector-borne viral disease having epidemic potential. Besides staggering human and economic costs, there has been a 30-times rise in disease incidence over the past 50 years. WHO declared dengue fever as the most common arthropod-borne communicable disease caused by four flavi viral serotypes through the transmission by female Aedes aegypti and Aedes albopictus.[2] An infected female mosquito can transmits any of the four viral serotypes to susceptible humans in one bite.[3,4,5] WHO estimates suggests that more than 100 million dengue infections may occur worldwide every year.

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Pakistan ranked sixth among most populous countries with estimated population of 207 million. In recent decades, considerable social changes have led to expeditious urbanization. Economic survey 2014 indicated the estimated nominal per capita GDP of US$1,197 with 21% of the people subsisting below the international poverty line of US$1.25 a day. Infectious and contagious diseases pose a heavy burden on the health care system in Pakistan along with having a negative impact on socio-economic growth and productivity,[6] Among those, dengue is threatening lives of the millions of people because of its predominating distinct socio-economic conditions and definitive epidemiological position. First case of dengue fever was reported in 1985 followed by re-appearance in 1994 and 1995. Pakistan has faced several dengue outbreaks since then, worst being in 2011, costing hundreds of human lives. Dengue cases have been reached to an alarming level especially during post monsoon season and the disease has been declared endemic in Pakistan.[7] It was reported as an undifferentiated fever first time in 1985 in Pakistan affecting children under 16 years of age8. During the year 1995, 75 new cases of dengue were reported in Hubb, Baluchistan[1] followed by 1000 infections and 7 deaths in Haripur while 2500 cases reported in Khushab, Nowshera with 11 deaths among those infected individuals during the year 2003. In 2004, 25 cases were declared from Karachi and Islamabad while in 2005, 13 patients died out of 500 dengue infected cases in Karachi. The year 2006 brings 5400 dengue cases from Karachi, Sukkar, Nawabshah, Rawalpindi and Islamabad and 55 deaths reported.[10,11] In 2007, dengue again affected Karachi, Hyderabad, Mirpurkhas, Lahore, Haripur, Rawalpindi and Islamabad, and 2700 cases were highlighted along with 24 deaths. In 2008, there was high frequency of DHF in Lahore with 1800 positive cases for dengue. In 2009, overall 570 cases while in 2010, 5000 positive cases were documented. In Khyber Pakhtunkhwah and Azad Jammu Kashmir, 25 and 5 cases were stated from both areas, respectively. Pakistan had faced the worst outbreak of dengue in 2011. More than 20,000 people were affected and resulted in 300 deaths according to official reports. Majority of the cases were observed in Lahore followed by other cities of Punjab including Faisalabad, Rawalpindi and Sargodha.[12] In Karachi, Sindh 196 cases were recorded. Various researches have shown that there is a need to give awareness and knowledge to the people of different preventive practices for combating dengue effectively. Television/Radio plays the important role in conveying health information to the population. But due to poor financial condition all cannot buy TV/Radios and newspapers for information so effective campaigns must be done.[13] The purpose of this study is to assess knowledge, attitude and practices of community regarding dengue prevention and control, Community perception regarding dengue fever and their behavior of adapting general preventive strategies .

METHODOLOGY

A cross sectional study was conducted to assess the knowledge ,attitude and practices of the community members visiting the government health facilities of primary and secondary level for reasons other than dengue fever at district Rawalpindi during a period of 6 months March 2019 to Sept 2019. Primary source of data collection has been used. This data has been collected by face to face interviews with the help of a framed open ended questionnaire. Sample size was taken as 310 calculated by open epi software at 95% confidence interval and at 5% margin of error, taking frequency of anticipated factor i.e knowledge of dengue among population as 72%.[14] Sampling was done through multistage sampling in which facility based selection was done through stratified sampling technique out of 118 health facilities 31 facilities were recruited including 3 District level hospitals, all RHCs and THQs and 2 BHUs from each tehsil. We selected 10 Community members through simple random sampling from each health care facility and total community members from 31 facilities were 310 .

RESULTS

A total of 310 community members were randomly selected and interviewed, who were visiting health facilities for reasons other than dengue. 10 community members were selected from each facility in which both man and women of different age groups were observed visiting health facility. Maximum were females 73.55%(228). Majority of the participants were of the age group 20-50yrs 62.90% (195), while minimum above 50 years of age 4.19%(13).Most of the community participants had matric level education representing 33.55%(104). Only 2.58% had graduate level education.(Table 1). All community participants recruited in the study (100%) knew about this disease. Majority of them 76.1% know about the disease from their family, friends, neighbors or teachers. Those learn from doctors were 23.9%. Only 1 respondent shared that there is someone infected with the disease in his/her close vicinity that is his/her neighbor/friend and that person immediately contacted health facility for treatment. 41.3% respondents reported using bed nets while 58.7% people had not adopted that protection measure. 40.6% people among 128 participants revealed that they self purchased the bed nets. Only 2(0.6%) said that government provided these bed nets. Moreover, according to 41.3% people recruited in study, bed nets they used were not impregnated. The reasons for not using bed nets include un affordability (20.3%), hot weather (8.1%), and unpleasant smell (1.9%) (Table 2).

All Community members who visited the health facility for the reason other than dengue only 1% witnessed organization of awareness campaigns in their areas by government Health Team. They were also asked to provide some suggestions for dengue prevention and control. Majority (62.6%) suggested keeping environment clean and (9.7%)

Table 1: *Demographic Profile of Community Participants*

Characteristic	Frequency (N=310)	Percentage (%)
Gender		
Male	82	26.45
Female	228	73.55
Age Groups (Years)		
15-29	102	32.90
20-50	195	62.90
Above 50	13	4.19
Education		
Not Literate	33	10.64
Under Primary	56	18.06
Under Matric	53	17.09
Matriculate	104	33.55
Intermediate and above	64	20.64
Type of Health Facility		
DHQ	10	3.22
THQ	60	19.35
RHC	80	25.81
BHU	140	45.16
THQ	20	6.44
Respondent by Tehsil		
Gujjar Khan	60	19.35
Kahutta	30	9.68
Kallar Sayean	30	9.68
Kotli Sattian	40	12.90
Murree	40	12.90
Rawalpindi	80	25.81
Taxila	30	9.68

Table 2: *Health Care Seekers Awareness Regarding Dengue Prevention and Control*

Variables	Awareness	Frequencies	Percentages
Knowledge about disease	YES NO	310	100
Source of information	Peers (Family, Friends,Teacher, Neighbor)Doctor	235 75	76 24
Health facility reported in case of illness	Govt. hospitals RHC/BHU/ Dispensary Private hospitals/ clinic	90 219 1	29 70.6 0.3
Total		310	100
Adequate treatment provided	YES NO	280 30	90 10
Free of cost treatment provided	YES NO	307 3	99 1
Use of bed nets	YES NO	7 303	2.3 97.7
Reasons for not using bed nets	Affordability Feel heat Feel smell Other	106 75 3 119	35 24.7 1 39.3
Total		303	100
Awareness campaigns held in the community	YES NO	100 Nill	100

said to provide proper sanitation facilities, (16%) suggested for proper water drainage, (3.9%) suggested that there should be regular spray, (2.3%) gave importance to the use of bed nets, (0.6%) gave importance to the use of quil and lotion and (4.5%) suggested for the use of safe water (Table 3).

DISCUSSION

The study has been conducted in district Rawalpindi, located in the northernmost part of the Punjab province of Pakistan. Dengue is major public health concern of this area. The number of patients affected by dengue virus has reached to an alarming figure of 3600 during 2017. Moreover, six deaths from dengue fever have also been reported in Rawalpindi District.[16]

Table 3: Suggestions for Dengue Prevention and Control

	Frequency	Percent	Valid Percent	Cumulative Percent
No Answer	51	16.5	16.5	16.5
Keep clean your place	24	7.7	7.7	24.2
Keep environment neat and clean	194	62.6	62.6	86.8
Need more awareness	3	1	1	87.7
Need proper sanitation	30	9.7	9.7	97.4
Need Sanitation	1	0.3	0.3	97.7
Use quil and lotion	2	0.6	0.6	98.4
Use quile	2	0.6	0.6	99
Use safe water	3	1	1	100
Total	**310**	**100**	**100**	

Community members visiting health facilities for reasons other than dengue fever were recruited in the study and majority among them was females. Similar study was conducted in Cambodia in which out Of 600 participants who were administered the KAP survey, the majority were female (77.8%),[2] This is suggestive of health seeking behavior of females because they are a vulnerable group and having a high level of physical, psychological, and/or social risk.

All respondents reported nearby health facility or hospital in their vicinity. Among those facilities, majority were BHU, RHC or Dispensary and according to them patients were provide suitable treatment in those health facilities. Majority of the participants told that these facilities are providing free of cost treatment.

These facilities were in close proximity to the residence of most community participants and it is usually easy for the females to approach these facilities for care seeking. Only small proportion of participants was not literate, otherwise maximum had matric level education. All these were well aware of the disease Majority of them know about the disease from their family, friends, neighbors, teachers or doctors. A sizeable proportion of the respondents were using personal prophylaxis measures against mosquitoes. However, a considerable number was not aware of preventive measures against mosquitoes at community level., this shows there were lack of awareness campaigns to raise the basic awareness level of public knowledge about dengue fever its prevention and control. A KAP survey together with an extensive entomologic survey was conducted in two subdistricts of Kamphaeng Phet province, Thailand.[17] To improve Community knowledge the awareness campaigns must be repeatedly organized by Government. Personal Protection is an important point in prevention from dengue fever as mosquito bite is the cause of disease transmission. In this study people were more focusing on the factors which are not cornerstone in the prevention of dengue fever e.g sanitation, clean environment and safe water supply, and were giving least importance to the personal protection factors that are directly concerned with dengue fever prevention e.g use of bed nets for protection against mosquitoes ,use of quil and lotions ,use of mosquito repellent sprays. It should be noted that people are largely unaware of tires and flower pots as being important breeding places for mosquitoes. Similarly, knowledge and use of interventions Beside poor knowledge about dengue fever some people were not using bed nets because of un-affordability, difficultly in using during summer season because of hot weather and unpleasant smell of these bed nets. These issues must be considered in awareness

campaigns. A study from Brazil on the public knowledge and attitudes concerning dengue found a gap between knowledge and practices about vector prevention.[18] Another study from Northeast Thailand identified several barriers towards dengue control including insufficient control agents and inadequate knowledge of control methods.[19] Swaddiwudhipong W et al have suggested that health education can induce the people to accept themselves as being responsible for Aedes control programs.[20] A study done in Puerto Rico regarding attitudes towards dengue prevention revealed that participants insisted that "neighbours" needed to control larval habitats, and the Government had the responsibility to fumigate.[21]

Based on our findings, it is recommended that future campaigns should involve more aggressive health education in cooperation with health workers and community schools. Audiovisual media can also be used as a tool to disseminate mass awareness.[22] Health education programmes should, therefore, deliver information in a more compatible sociocultural context for a friendlier and effective reception.[19] Capacity building is also an essential part for successful community participation.

This study not only provides important basic information among the community regarding dengue prevention and control but can also help to identify areas that can be targeted in future campaigns. The knowledge obtained from this study may can be used to monitor the effectiveness and progress of dengue prevention campaigns.

CONCLUSION

The knowledge and attitude of the respondents concerning dengue control was not satisfactory, people don't know that dengue mosquito bites at day time and breed in clean water. They were focusing more on the things which are not primarily concerned with dengue like sanitation and they were giving less importance to the personal protective measures e.g the use of bed nets ,use of anti mosquito lotions, use of quile, use of sprays which constitute cornerstone in dengue prevention and control. Adequate preventive practices and education can be achieved by improving the knowledge and awareness level of the people, particularly from rural and illiterate background is important. So the awareness educational campaigns should be designed to improve behavior and practices of prevention & control measures against dengue fever of the community.

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FREQUENCY OF THE HISTOLOGICAL GRADES OF ASTROCYTOMA: A STUDY IN A LOCAL POPULATION

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Abstract

Objectives: Astrocytomas are CNS tumors originating from astrocytic glial cells and oligodendrocytes which are predominant glia cells of the central nervous system. According to WHO criteria these tumors can be divided into four grades by the appearance of cellular atypia, mitosis, microvascular proliferation and necrosis. The current study is carried out to identify the incidence and trends of four grades of astrocytomas in local population.

Results: Out of total of 74 cases of all four grades of astrocytomas. Grade I astrocytomas were 9 (12.16%) grade II were 17 (22.97%), grade III were 21 (28.38%) and grade IV were 27 (36.49%). In this study, there were 74 patients suffering from different grades of Astrocytoma and amongst them there were 25 (33.78%) female patients and 49 (66.22%) were male patients resulting in female to male ratio 1:2.

Glioblastoma multiforme (grade-IV) was the most common tumor comprising a total number of 27 cases with a mean age of 43 yrs ±16.21 and with the male to female ratio of 2.37:1. Diffuse astrocytoma (grade II) was the next most common tumor comprising of total 21 (cases with a mean age of 35.52 ±13.19, accounting for male to female ratio of 1.62:1.Anaplastic astrocytoma (grade III) was the third most common tumor comprising a total of 17 cases with a mean age of 32.58 ±15.93 and with the male to female ratio of 3.25:1. Pilocytic astrocytoma was the least common astrocytomas and comprising of total 9 cases among all patients with a mean age of 16 ±3.16 and with the male to female ratio of 1.25:1

Methods: This cross sectional analytical study was done in Lahore General Hospital during period of one year.Eosin and hemotoxylin stained sections for different grades of astrocytomas were examined and frequency and percentage were calculated for histological grade of the tumor. Data was entered and analyzed through IBM SPSS 20 and were presented in frequency or percentage form.

Conclusion: The majority of the age group of patients who were diagnosed with astrocytomas were between 15 to 30 years and among these majority of the people showed high grade astrocytomas i.e anaplastic and glioblastoma mutltiforme.

Keywords: Astrocytomas, Pilocytic astrocytoma, Diffuse astrocytoma, Anaplasctic astrocytoma and Glioblastoma multiforme

Worldwide astrocytomas are the commonest brain tumors in both males and females.[1] It is also one of the leading causes of deaths in children.[2] Across the world, the total incidence of all types of brain tumors including astrocytomas, is approximately 13 people out of every 100, 000.[3]

Worldwide studies, particularly in Western countries, show that astrocytomas have male predominance.[4] In Pakistan one study reported a female to male ratio of 1:1.6 & 1:1.17 respectively.[5] In children and in older age patients low grade and high grade astrocytomas are more common respectively.[6] In Pakistan, data showed that the mean age for astrocytic tumors is 43.01 years.[7]

Patients of astrocytomas are associated with genetic diseases like Li-Fraumeni syndrome, nevoid

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basal cell carcinoma, neurofibromatosis, tuberous sclerosis, turcot sydrome and Von Hippel disease.[8]

The human brain is a complex structure, containing about 100 billion of neurons and many supportive cells like astrocytes, oligodendrocytes, microglial cells, ependymal cells and meningothelial cells.[9] Astrocytomas are developed from a particular kind of glial cells, that are stellate-shaped brain cells known as the astrocytes.[10] This cell surrounds the neurons, which provide oxygen, nutrients and remove dead cells, thus supporting and protecting the neurons[11]. They also support, protect and help in passing messages between the neurons. Therefore, astrocytes are essential in processing information in the brain.[12]

The astrocytic tumors are graded by the World Health Organization from I-IV, which is on the basis of the presence or absence of four histological features that are nuclear atypia, mitoses, micro vascular proliferation and necrosis.[13] Tumors graded I and II are slow-growing, and are referred to as low grade. Tumors graded III and IV are rapid-growing and more aggressive tumors, and referred as high grade, this means, their size increases more rapidly and sometimes metastasize to different parts of the brain or spinal cord.[13]

Grade I are known as pilocytic astrocytomas .The term "pilocytic" indicate cells with hair-like, bipolar processes.[14] One of its variants termed as "pilomyxoid astrocytoma" which is a rare tumor, occurs predominantly in children who are under one year of age and develops in the hypothalamic region.[15] Pilocytic astrocytoma is the most common pediatric brain tumor in Pakistan.[16]

In H & E staining, the microscopic features of (Grade I) astrocytoma shows long bipolar neoplastic cells with elongated hair-like processes & Rosenthal fibers and they are considered as low grade neoplasms.[17]

Diffuse astrocytomas (WHO Grade II) are also referred to as low grade astrocytomas. The most common histological subtype of diffuse astrocytoma is fibrillary astrocytoma.[18] Fibrillary astrocytomas are grade II, which are slow in growth, but may show progressive behavior to higher grade tumors.[19] Grade II astrocytomas can occur anywhere within the CNS but commonly occurs in supratentorial region.[20] The Peak incidence of grade II tumor is seen in adults between the ages of 30 to 40 years with male predominance of 1.18:1. Mean survival time following diagnosis of grade II astrocytoma is 6 to 8 years[21]. In microscopic examination after H & E staining, grade II astrocytomas show increased cellularity and mild nuclear atypia.[22]

The grade III astrocytoma is called an 'anaplastic astrocytoma'. They are also fast-growing and referred to as high grade malignant tumors. Following treatment, they can reoccur in a more advanced form i.e. grade IV astrocytoma which is also known as glioblastoma multiforme. They are more common in male adults between the ages of 30 and 70 years.[23] Five years survival rate of anaplastic astrocytoma in adults is approximately 14%.[24]

Microscopic examination of grade III astrocytoma shows increased mitotic activity, marked nuclear atypia and endovascular proliferation.[25]

The highest grade astrocytoma (grade IV) is Glioblastoma multiforme, which is abbreviated as "GBM".[26]

The malignant nature of astrocytomas makes it the fourth greatest cause of cancer death[27]. The histopathological features that differentiate glioblastoma multiforme from all other three grades of astrocytomas, are the presence of necrosis and increase of unusual increase growth of blood vessels around the tumor.[28] Among all gliomas, GBM is the most aggressive of all primary tumors of the brain with worse prognosis.[29] Patients may live for years with low grade gliomas, but high grade are usually fatal within two years with treatment and often within weeks if untreated. The prognosis of patients with high-grade astrocytomas is very poor. It has a mean survival rate of 10 to 12 months.[30]

On microscopic examination after H & E stai-

ning grade IV astrocytomas show marked pleomorphism, nuclear palisading around necrosis and endovascular proliferation and giant cells.[31]

The symptoms of astrocytic tumors depend on the site of the tumor and also whether there is increased pressure in the head or it's normal. These symptoms include nausea, vomiting, irritability, lethargy, clumsiness, fits, changes in personality, abnormal gait and difficulty with tasks like handwriting.[32]

METHODOLOGY

Sample size of 74 cases was calculated with 95% confidence interval. This cross-ectional study was carried out at Post Graduate Medical Institute (PGMI), 06 Abdul Rahman Chughtai Road, Lahore. Lahore General Hospital Non-probability/ purposive sampling. Technique was used for sample collection.

SAMPLE SELECTION:

INCLUSION CRITERIA:

- Freshly diagnosed cases of astrocytomas were included.
- Patients of both gender and all ages were included.

EXCLUSION CRITERIA:

- Patients with recurrent tumors.
- Patients on chemotherapy or on radiotherapy.

TISSUE PROCESSING & CUTTING:

After surgical procedures, specimen were fixed in 10% neutral buffer solution and brought into the histopathology laboratory. These were allocated a laboratory number.

On first day the specimen was fixed for 24 hrs. Small fragments of tissue or a stereotactic core needle biopsy was measured, grey and white matter was identified if distinguished.

A careful gross examination was done and features were noted according to standard guidelines.[33]

The small fragments of brain for permanent sections were wrapped in saline moistened lens paper and passed entirely. The fragments were handled gently as there was little supporting tissue. The small biopsy pieces were processed in an automated processor for 20 hours.

The processing of the sections included dehydration by ethyl alcohol, clearing by xylene, and impregnation by paraffin. After processing paraffin embedded tissue blocks were prepared.

The tissue sections 3-4µm thick were obtained by use of rotary microtome. The sections were mounted on glass slides and dried completely at 60 Cº for 30 minutes. Hematoxylin and Eosin staining of the sections was done as per standard protocol.

After staining, slides were examined under Olympus BX-40 binocular microscope.

The diagnosis was made in each case and grading was done according to WHO Grading Scheme[34] (Louis et al., 2007).

The old WHO grading scheme is based on the presence or absence of four histological parameters.[35]

1. Nuclear atypia: Defined as nuclear pleomorphism and hyperchromasia.
2. Mitosis
3. Microvascular Proliferation**:** Endothelial proliferation within the lumen of blood vessels.
4. Necrosis, Coagulative, Pseudopalisading

- WHO grade II tumors (diffuse astrocytoma): Show only nuclear atypia
- WHO grade III tumors (anaplastic astrocytomas): Show nuclear atypia and mitosis.
- WHO grade IV tumors (glioblastoma): Show nuclear atypia, mitosis, micro vascular proliferation and necrosis.

Statistical Methods:

Data was entered and analyzed through IBM SPSS 20 and was presented in frequency or percentage form.

Ethical Consideration:

The study was started after taking approval from ethical committee and making sure that there was no ethical issue involved in this study. Health of

patient was prior consideration and confidentiality of patients information was assured and maintained.

RESULTS

In this study, there were 74 patients suffering from different grades of Astrocytoma and amongst them there were 25 (33.78%) female patients and 49 (66.22%) were male patients resulting in female to male ratio 1:2.

Mean age of the patients was 35.45±16.488 years with minimum age of the patient was 12 years and maximum age of the patient was 68 years (Fig 5).

There were 9 (12.16%) patients who were between 1 to 15 years, 28(37.8%) were between 15 to 30 years, 17(22.9%) were found between 30 to 45 years, 13 (17.56%) were in the range of 45 to 60 years and 7(9.45%) were seen between 60-75 years of age (Fig 6).

Headache, motor function loss, vomiting, and giddiness were the main presenting complaints in the descending order of frequency (Table 1).

CT scan and MRI findings showed that about 41(55.4%) tumors had hemorrhage, 38(51.3%) showed necrosis, 43(58.1%) lesions presented with cystic changes and 20(27.02%) showed calcification.

The most common biopsy received was stereotactic, which was performed in 30 cases out of 74(40.5 %) patients of astrocytomas (Table 2).

The majority tumors were high grade i.e. 44 cases out of 74 (59.46%) and low grade were found in 30 out of 74 (40.54%).

Out of 74 cases, 9 were pilocytic astrocytomas (12.16 %), 17 were diffuse astrocytomas (22.97%), 21(28.38%) showed features of anaplastic astrocytomas and 27 (36.49 %) were of glioblastoma multiforme (Figure 5).

Glioblastoma multiforme (grade-IV) was the most common tumor comprising a total number of 27 cases with a mean age of 43 yrs ±16.21 and with the male to female ratio of 2.37:1. Diffuse astrocytoma (grade II) was the next most common tumor comprising of total 21 (cases with a mean age of 35.52 ±13.19, accounting for male to female ratio of 1.62:1. Anaplastic astrocytoma (grade III) was the third most common tumor comprising a total of 17 cases with a mean age of 32.58 ±15.93 and with the male to female ratio of 3.25:1. Pilocytic astrocytoma was the least common astrocytomas and comprising of total 9 cases among all patients with a mean age of 16 ±3.16 and with the male to female ratio of 1.25:1 (Table 3 and Table 4).

Statistical Analysis:

No significant associations were seen between the clinical variables (age, symptoms, gender, site etc) applying chi square test ($p \leq 0.05$).

DISCUSSION

In this study total patients were 74 patients, out of them 25(33.78%) patients were female and 49 (66.22%) were male patients with female to male ratio 1:2. These results share common features with the study performed by Ramachandran et al.[36] (2017). This study showed that the total female patients were 32% and males were 62% in the sample size of 89 patients in their local population. Other studies also showed slight variation to these results,[37,38] who reported a female to male ratio of 1:1.6 and 1:1.17 respectively. Grimm and Pfiffner (2013)[39] showed opposite results with female to male ratio of 2:1. This difference could likely be because of demographic variation in the local population.

In this study the mean age of the patients was 35.45±16.488 years with minimum age of the patient was 12 years and the maximum age was 68 years. Similar results were reported by Dong et al. (2014).[40] They reported that the mean age of patients with astrocytomas in their respective population was 44 years, minimum age was 10 whereas maximum was 77 years. Slightly higher results were shown by Schiff.[41] (2015) who studied a local population of low grade astrocytomas with a mean age of 36 years and slightly lower results were shown by Motomura et al.

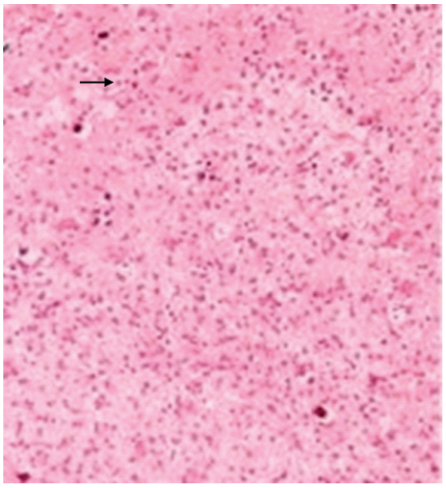

Fig 1: *Grade I astrocytomas in H& E staining. (Black Arrow Showing Fibrillary Background, Green Arrow showing Bipolar Cells with Hair like Processes)*

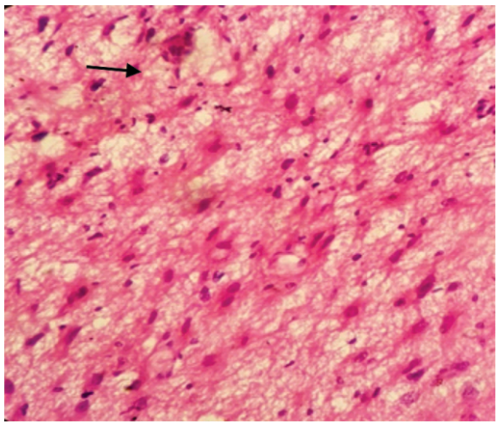

Fig 2: *Grade II Astrocytomas in H& E Staining, (Black Arrow showing Mild Nuclear Atypia)*

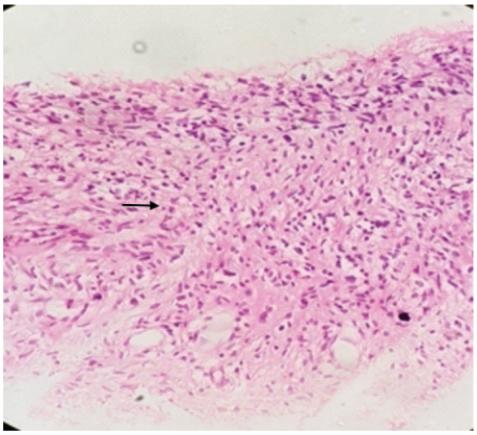

Fig 3: *Grade III Astrocytomas in H& E Staining. (Black Arrow showing Increased Mitotic Activity,Red Arrow showing Marked Nuclear atypia).*

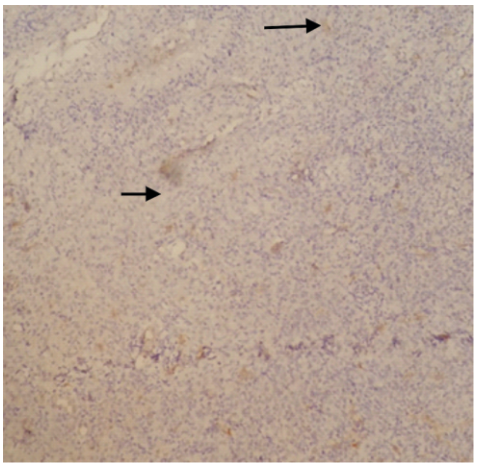

Fig 4: *Grade IV Astrocytomas in H& E Staining., (Red Arrow showing Marked Pleomorphism, Black Arrow Showing Necrosis)*

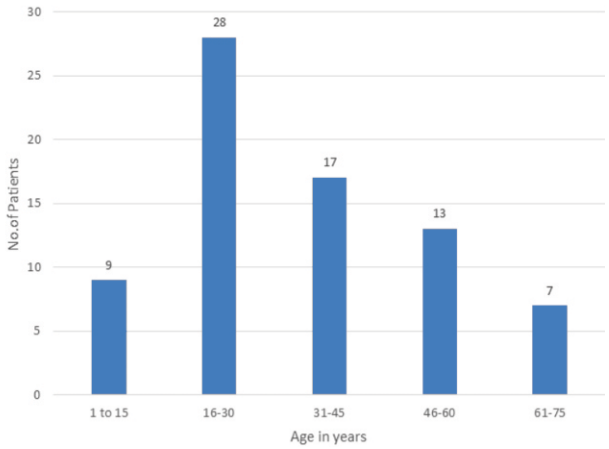

Fig 5: *Frequency Distribution of Age of Patients*

Table 1: *Frequency Distribution of Presenting Complaints for Patients of Astrocytomas*

Symptoms	Responses	
	Number of patients(N)	Percent
1. Headache	72	30.8%
2. Motor function loss	70	29.9%
3. Vomiting	61	26.1%
4. Giddiness	31	13.2%

Table 2: *Frequency Distribution of Biopsy Procedure for Astrocytomas*

Biopsy	Frequency	Percent
Burrhole	20	27.0
Stereotactic biopsy	30	40.5
Open biopsy	24	32.4
Total	74	100.0

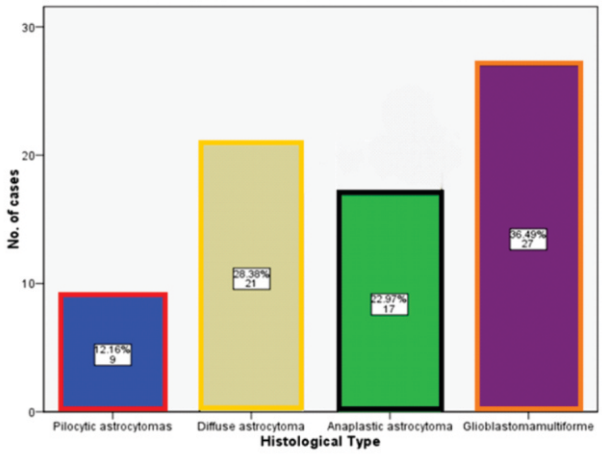

Fig 6: *Frequency Distribution of Four Histological Grades of Astrocytomas*. (2013)[42] in which the mean age of 34.5 years. The difference can be linked to difference in genetic makeup and races.

Table 3: *Frequency Distribution of Patients of all Four Grades of Astrocytomas with Respect to Age Groups of Patients*

Age	Total no. of patients	No. of patients for grade I	No.of patients for grade II	No. of patients for grade III	No. of patients for grade IV
1-15 years	9	6	0	2	1
15-30 years	28	3	9	8	8
30-45 years	17	0	9	4	4
45-60 years	13	0	3	2	8
60-75 years	7	0	0	1	6
Total	74	9	21	17	27

Table 4: *Frequency Distribution of Grades of Tumor in Accordance to Gender*

Grades of astrocytoma	No. of male patients	No. of female patients	M:F	Total
I	5	4	1.25:1	9
II	13	8	1.62:1	21
III	13	4	3.25:1	17
IV	19	8	2.37:1	27

In the present study out of 74 cases, 9(12.16%) were of pilocytic astrocytomas, (22.97%) showed diffuse astrocytomas, 21(28.38%) were of anaplastic astrocytomas and 27(36.49%) cases were of glioblastoma multiforme. According to Wen and Kesari (2008)[43] glioblastoma multiforme accounted for 60-70 % of all the astrocytic tumors. However, in the study of Thakkar et a, (2014)[44] found that glioblastoma multiforme accounted for 50% of all astrocytic tumors. GBM is the most common brain tumor in the present study as well. A study from Agha Khan University Hospital Karachi reported that the grade-III and grade-IV astrocytomas accounted for 60.41% of the astrocytomas[45] and these results are similar to our study.

Out of 74 cases of astrocytomas 9(12.16%), (22.97%), 21(28.38%) and 27(36.49%) cases were of pilocytic astrocytomas, diffuse astrocytomas anaplastic astrocytomas and glioblastoma multiforme respectively. According to, pilocytic astrocytomas accounted for 7.97% and diffuse astrocytomas comprised of (13.13) % which fell in lower limits when compared with our study.This difference could be due to demographical changes. According to the same study, anapalstic astrocytomas comprised of 29.89 % and glioblastoma multiforme constituted 70.11%. These results found to be in close agreement with our study. These results also showed that glioblastoma multiforme is the most frequent brain tumor accounting for 60 to 70 % of all the astrocytic tumors.[48] A study from Tertiary Care Hospital Peshawar and University Hospital Karachi reported that the grade-III and grade-IV astrocytomas accounted for 55% and 60.41% respectively of all grades of the astrocytomas.[49] These findings were similar to the study of Lourenco et al. (2016)[50] who observed that the patients of pilocytic astrocytomas were about 13.18 %, which was slightly higher than our result. Collins and Christo foridis(2016)[51] noted that diffuse astrocytomas account for 22% in their local population which was almost same to our study.

The results of the present study related to the size of the tumor and other gross features were also in concordance to the results of the study performed by Ahmed et al. (2015)[52]

The features showed on MRI and CT scan of this study are almost similar to the study done by Upadhyay et al(2011).[53]

In the current study 37.8% of the astrocytomas occurred mostly in the 3rd decade of life followed by

22.9% and 17.56% in 4th and 5th decades respectively. In comparison to the most series reported from Asian countries,[54,55] brain tumor occurred mostly during the 4th decade of life. This contradiction with this study could be due to difference of availability of various diagnostic techniques. A study from Pakistan stated that intracranial brain neoplasms had mostly occurred in the 3rd decade of life which concided with this study.[56]

The mean age of patients with Pilocytic astrocytomas in the current study was 16 ±3.16 with the male to female ratio of 1.25:1 which was slightly higher as compare to the results of the study done in Pakistan in which the mean age of patients of pilocytic astrocytomas was 9.25 with the female to male ratio of 1:1 but in adults pilocytic astrocytomas show male predominance57 (Khan et al., 2012).

Diffuse astrocytomas (grade II) is the next most common tumor in our study and comprised of total number of 21 cases with a mean age of 35.52 ±13.19. The study by Lind-Landstrom et al (2012)[58]. showed slightly higher results with the mean age of 40 years but this fell in the same decade of life. Results about age of patients concluded by Sarica et al(2012)[59] were higher as compared to our study regarding anaplastic astrocytomas. They found that the mean age of the patients was 49±13.6 with male: female ratio was 1.85:1 while the total number of patients of anaplastic astrocytomas was 17 with a mean age of 32.58±15.93 with the male to female ratio of 3.25: 160. Glioblastoma multiforme is primarily diagnosed at an older age with a median age of 64 years old at the time of diagnosis.[61,62] The incidence increased with age and a peak incidence was between 75 to 84 years which droped after 85 years.[63] The age at the time of diagnosis was likely to be higher for primary cases of glioblastoma multiforme (mean age of 55 and median age of 64, male-to-female ratio of 0.65:1). These results were almost similar to the current study which has showed that the patients with glioblastoma multiforme had the mean age of 43 years ±16.21 with the male to female ratio of 2.37:1.

Headache, motor function loss, vomiting, and giddiness were the main presenting complaints of patients having astrocytomas. Results of Study carried out by Subirana Domènech et al. 2001,[64] were in close agreement with the present study. In another study motor loss with severe headache were the prominent clinical features of patients with astrocytomas.[65]

In other studies, the most common brain biopsy taken for diagnosis was stereotactic type,[66,67] these results concides with the current study. An old study done by Silverman (1986)[68] showed much lower results and was not comparable with the present study. He showed that only 5 cases were diagnosed with different types of brain tumors through burr hole biopsy including anaplastic astrocytomas.

The majority tumors in our study were high grade i.e. 44 cases out of 74(59.46%) and low grade were 30 out of 74(40.54%). Similar results were reported by Dong et al 2009[69] and glioblastoma multiforme was the most common astrocytomas,[70,71] while Pilocytic astrocytomas was the least common tumor.[72] Diffuse astrocytomas occured as the 3rd most common tumor among all astrocytomas,[73] which was similar to the current study.

CONCLUSION

Majority of the patients in local population was suffering from high grade astrocytomas and high grade astrocytomas were mostly seen in male patients.

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ASSOCIATION OF CHRONIC URTICARIA IN CHILDREN WITH WORM INFESTATION

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Abstract

Objectives: chronic urticaria is a disorder characterized by wheal formation, angioedema or both for longer than 6 weeks. There is itching, swelling and redness. Daily working and sleep can be affected by severe itching. It can be caused by cold, heat, water, pressure, and infections including worm infestation.

Methods: We conducted a prospective study from December, 2018 to May, 2019. Data analysis was done by Statistical Package for the Social Sciences (SPSS) Version 20 and expressed as frequency and percentage.

Results: Total number of patients with chronic urticaria was 250, of which 139 (55.6%) were males and 111 (44.4%) were females. Fifty-four patients (21.6%) with chronic urticaria had worm infestation, and 196 (78.4%) did not have. Of those who had worm infestation, 34 (26.3%) were males and 20 (18.01%) were females. The ages of the patients were from 0-18 years. Maximum number of cases (38.4%) of chronic urticaria were seen in 13-18-year age group. Whereas maximum number of cases (23.80%) with worm infestation were seen in 7-12-year age group.

Conclusion: Chronic urticaria is a common condition and in 26.3% cases it is associated with worm infestation. So, we should routinely do stool examination in every case of chronic urticaria.

Key words: Chronic urticaria, Angioedema, Worm infestation

Urticaria is a common condition that affects 15-25% people at some time in their life. It can be acute or chronic. The lesions can vary in size from few millimeters to a few centimeters.[1] Chronic urticaria is a disorder, in which there is wheal formation, angioedema or both for longer than 6 weeks. It is characterized by degranulation of cutaneous mast cells leading to release of different mediators, like histamine and others that result in swelling, itching and redness.[2] Daily working and sleep can be impaired by severe itching.[3]

Histologically, wheals show edema of dermis, vasodilation and increased vascular permeability. Same changes are seen in lower dermis and subcutaneous tissue in angioedema.[4]

Chronic urticaria can be classified as chronic spontaneous urticaria and inducible urticaria. Urticaria can be induced by cold, heat, sun exposure, water, sweating, pressure, contact, drugs, vibration and infections.[5,6] Parasites can also cause chronic spontaneous urticaria in children and remissions occur after deworming the patient.[7] Infections with endoparasites such as helminths and protozoa cause chronicurticaria. Overcrowding, poor socioeconomic conditions, poor sanitation predispose to parasitic infections.[8]

OBJECTIVE

The aim of the present study is to evaluate the frequency of worm infestation in patients with chronic urticaria.

METHODOLOGY

This was a prospective study conducted at

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Department of Dermatology, Sargodha medical college, Sargodha, from January, 2018- May,19. In clinically diagnosed cases of chronic urticaria, stool examination was done for three consecutive days by formal ether concentration method for ova, cyst or parasite. The patient was considered to be free of worm infestation if stool examination report was negative for worm, cyst or ova for three consecutive days. Patients consent was taken and data was entered in proforma.

Inclusion Criteria: All the clinically diagnosed cases of chronic urticaria of both sexes and ages 0-18 years were included in the study.

Exclusion Criteria: Patients above 18 years of age and with fungal, viral or bacterial infection were excluded from the study. Institutional ethical approval was taken (UMC & RC 28).

The data was expressed as frequency and percentage and analyzed using SPSS (Statistical Package for the social sciences) Version 20.0 (SPSS for Windows, SPSS Inc., Chicago, IL, USA).

RESULTS

The study was conducted from December, 2018-May, 19 in Department of Dermatology, Sargodha medical college, Sargodha. Study duration was 6 months. Total number of patients with chronic urticaria was 250, of which 139 (55.6%) were males and 111 (44.4%) were females (Figure 1, 2). Male to female ratio was 1.25:1. Fifty-four patients (21.6%) with chronic urticaria had worm infestation, and 196 (78.4%) did not have (Table 1). Of those who had worm infestation, 34 (26.3%) were males and 20 (18.01%) were females (Table 2). The ages of the patients were from 0-18 years. Maximum number of cases (38.4%) of chronic urticaria were seen in 13-18-year age group. Whereas maximum number of cases (23.80%) with worm infestation were seen in 7-12-year age group (Table 3).

Table 1: *Frequency of Worm Infestation in Patients with Chronic Urticaria*

Worm infestation	N
Present	54 (21.6%)
Absent	196 (78.4%)

Table 2: *Stratification for Gender in Patients with Worm Infestation*

Gender	Worm infestation	
	Seen	Not seen
Male	34 (26.3%)	95 (73.6%)
Female	20 (18.01)	91 (81.98%)

Table 3: *Stratification for Age in Patients with Worm Infestation*

Age (years)	Total patients	Worm infestation	
		Seen	Not seen
0-6	66 (26.4%)	14 (21.22%)	52 (78.78%)
7-12	88 (35.2%)	21 (23.80%)	67(76.13%)
13-18	96 (38.4%)	19 (19.79%)	77 (80.21%)

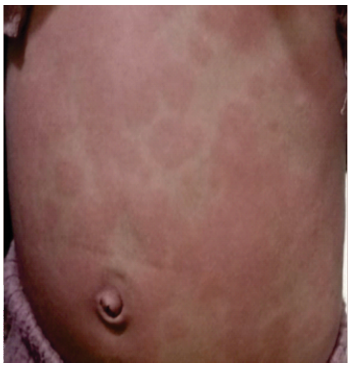

Figure 1. *Serpiginous Urticarial Plaques*

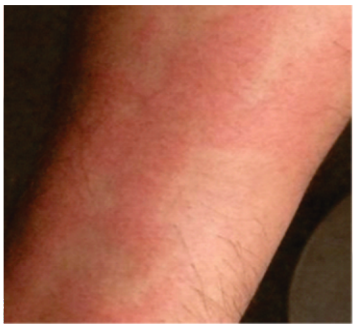

Figure 2. *Urticarial Plaques on Forearm*

DISCUSSION

Total number of patients with chronic urticaria was 250, of which 139 (55.6%) were males and 111 (44.4%) were females (figure 1, 2). Male to female ratio was 1.25:1. Study by Chansakulporn S et al (2014) showed chronic urticaria in 53% females. Fifty-four patients (21.6%) with chronic urticaria had worm infestation, and 196 (78.4%) did not have

(table 1).Work done by Kataria Uet al (2015) shows worm infestation in 58% patients of chronic urticaria. Of those who had worm infestation, 34 (26.3%) were males and 20 (18.01%) were females (table 2). The ages of the patients were from 0-18 years. Maximum number of cases (38.4%) of chronic urticaria were seen in 13-18-year age group. Lee SJ et al (2017) found the prevalence of chronic urticaria in 4-12-year-old children. Whereas maximum number of cases (23.80%) with worm infestation were seen in7-12 year age group (table 3).SedatVeziret al (2019) found worm infestation in 22.3% of patients with chronic urticaria in age up to 18 years.

It is concluded that chronic urticaria is a common condition and in 26.3% cases it is associated with worm infestation. So, we should routinely do stool examination in every case of chronic urticaria.

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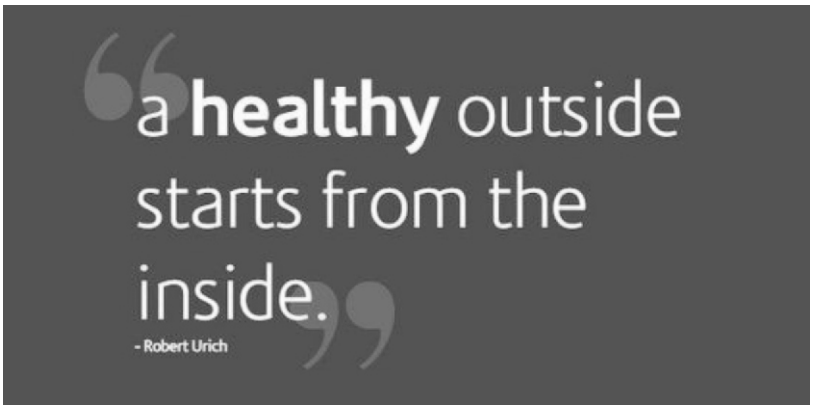

FREQUENCY OF INTERFERON RELATED VISUAL ACUITY PROBLEMS IN PATIENTS OF CHRONIC HEPATITIS C

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Abstract

Introduction: Retinopathy is a well recognized side effect of interferon therapy for treatment of hepatitis Cand surveillance for this side effect of interferon has not been done strictly in the past, but the consequences in terms of blindness demand that all patients receiving interferon therapy should have regular ophthalmologic examination so that permanent visual impairment can be prevented.

Objective: To elucidate the frequency of retinopathy in patients of chronic hepatitis C who are on conventional interferon alpha- ribavirin combination therapy.

Study Design: Descriptive case series.

Setting: Hepatitis Clinic, Medical Unit II, Jinnah Hospital Lahore.

Duration of Study: 25th Jan 2018 to 25th July 2018.

Methods: One hundred and fifty patients meeting the inclusion criteria were included in the study. Interferon and ribavirin combination therapy was then started in the dose of 3 million units subcutaneously thrice a week and 400mg orally thrice a day respectively. Fundoscopy was done by a single ophthalmologist in every patient after the week 6 and 12 of the start of therapy. Presence or absence of retinopathy was documented.

Results: One hundred and sixteen (77.3%) did not develop any retinal changes but remaining 34 patients (22.7%) suffered from retinopathy. (38.2%) had retinal hemorrhages and 21 (61.8%) had cotton wool spots. 14(41.2%) developed retinopathy during the first 6 weeks and 20 patients (58.8%) during the 7-12 weeks period of INF therapy. Cotton wool spots and retinal hemorrhages were noted in 6 (4%) and 9 (6%) asymptomatic patients respectively in 15 (10%) and 4 (2.7%) patients respectively who complained of reduced vision. Ten patients (6.6%) complaining of watery eyes had normal fundoscopy.

Conclusion: It is concluded from the study that every patient on interferon therapy should have regular eye examination for surveillance of retinopathy to prevent blindness, a dreadful consequence.

Key Words: Interferon, Retinopathy and chronic hepatitis C

Chronic hepatitis C causes cirrhosis of liver in 20% of the total 170 million people affected and is the commonest cause of hepatocellular carcinoma as well.[1] Treatment of hepatitis C with interferon-ribavirin combination therapy has proved efficacy in terms of biochemical and virological response.[2] Interferon is an anti-inflammatory, antitumor, antiviral, and immunomodulatory cytokine. Ribavirin is an antiviral agent with immunoregulatory activity.[3]

Various adverse effects of interferon include flu like illness, bone marrow suppression, thyroid dysfunction, depression, arthralgias and significant retinal complications[1]. Interferon induced retinopathy is characterized by retinal hemorrhages, cotton wool spots around optic disc, and macular edema. Branch retinal vein occlusion, retinal rubeosis and ischemic optic neuropathy are its rare manifestations.[4]

Interferon induced retinopathy ranges from completely asymptomatic condition to permanent visual loss.[5,6] These retinal changes most often develop within the first 12 weeks of interferon therapy.[7] Immune complex deposition in the retinal capillaries and ischemic insult similarly found in diabetes and hypertension are the proposed mechanisms underlying the development of interferon induced retino-

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pathy.[7]

Ocular side effects of ribavirin are mild watery eyes and conjunctivitis but it may also contribute in the development of interferon induced retinopathy and needs further investigation.[1]

A large scale study to determine the incidence of interferon induced retinopathy is yet to be done but various small scale studies conducted worldwide report its incidence between 19-64% depending upon the number of patients enrolled.[1,7]

Aim of the present study was to determine the frequency of interferon induced retinopathy in patients of chronic hepatitis C in Pakistani population and if it is found high, routine fundoscopic examination of such patients should be undertaken during interferon treatment. It will help in early recognition of retinopathy and permanent visual impairment can thus be prevented by timely holding interferon therapy and referral to ophthalmologist.

OBJECTIVE

To elucidate the frequency of retinopathy in patients of chronic hepatitis C treated with conventional interferon alpha-ribavirin combination therapy.

Retinopathy: was defined as patients having retinal hemorrhages, cotton wool spots, macular edema on fundoscopy was done after 12 weeks of the start of interferon therapy among patients with Chronic Hepatitis C determined on PCR essay.

METHODOLOGY

A case series study was conducted in Hepatitis Clinic, Medical Unit II, Jinnah Hospital Lahore from 25th Jan 2018 to 25th July 2018. One hundred and fifty patients of chronic hepatitis C were included in this study through a non probability purposive sampling technique. Sample size was calculated with 95% confidence level, 6% margin of error and taking expected percentage of interferon induced retinopathy i.e. 16 % at 12 weeks after therapy. Patients of chronic hepatitis C confirmed on PCR essay of either gender between ages of 20-50 years having normal fundoscopic examination before the start of interferon therapy were included in study and patients with diabetes mellitus diagnosed by history and fasting blood sugar level of >110 mg/dl for three consecutive mornings, with hypertension diagnosed by history and blood pressure readings of > 130/80 mmHg for three consecutive days previous history of eye trauma or surgery and laser phototherapy were excluded. Interferon and ribavirin combination therapy was then started in the dose of 3 million units subcutaneously thrice a week and 400mg orally thrice a day respectively. Fundoscopy was done by a single ophthalmologist in every patient after the week 6 and 12 of the start of therapy. Presence or absence of retinopathy was documented on the proforma (attached). Data was analyzed on SPSS version 12.0. Age was the quantitative variable and its mean and standard deviation were calculated. Gender and presence or absence of retinopathy was qualitative variables and values were expressed as frequencies and percentages.

RESULTS

Out of total 150, 88 patients (58.7%) were male and 62 were female (41.3%), (table1).71 patients (47.3%) had their ages in the range of 20-35 years. 79 patients (52.7%) were between 36-50 years. Mean age was 37 ± 7.907 years. 34 (22.7%) developed retinopathy. Out of the total 34 patients who developed retinopathy, 13 patients (38.2%) had it in the form of retinal hemorrhages and 21 patients (61.8%) developed cotton wool spots. No patient suffered from macular edema. 106 patients (70.7%) had no complaints and had normal fundoscopy. Six patients (4%) developed cotton wool spots but did not report any complaints. Nine patients (6%) developed retinal hemorrhages without any subjective complaints. Fifteen patients (10%) complaining of reduced vision were found to have cotton wool spots and 4 patients (2.7%) who developed hemorrhages experienced reduced vision. Ten patients (6.6%) with normal fundoscopy had watery eyes only.

DISCUSSION

Chronic hepatitis C affects more than 170 million people in the world.[10,11] Its prevalence in Pakistan estimated by various studies is betwen 3-13%.[12,13]

The treatment of chronic hepatitis C (CHC) is now well established with conventional interferon or pegylated interferon in combination with ribavirin.[14] Ocular toxicity is one of the dreadful complications of interferon therapy and the most common being ischemic retinopathy is characterized by hemorrhages and cotton wool spots. Other features include optic disc hyperemia and macular edema.[48-55]

Out of 150 enrolled patients in the present study, 88 patients (58.7%) were male and 62 (41.3%)

Table 1: Demographic and Clinical Chracteristics

Variable n= 150	Frequency	Percentage
Gender		
Male	88	58.7
Female	62	41.3
Age		
20-35	71	47.3
36- 50	79	52.7
Retinopathy		
Yes	34	22.7
No	116	77.3
Fundoscopy Finding n = 34		
Retinal hemorrhages	13	38.2
Cottonwool spots	21	61.8

female. This difference in number of patients with respect to gender is reflected in various studies conducted worldwide, where male patients were in overwhelming majority.[4] This difference may further strengthen the fact that male population seeks health care facilities with increased frequency in Pakistan.[69] Ages of the patients varied between 20-50 years. The mean age was 37 years which was well in accordance with internationally published study.[58] In this study 34 patients (22.7%) developed retinopathy with INF therapy, supporting further the already established fact by different studies conducted worldwide[57,58]. The incidence of reported retinopathy in patients receiving INF therapy is variable in different small scale studies to large study groups.[49] In this study group most of the patients were asymptomatic. The patients who did experience subjective complaints spoke of reduced vision and watery eyes. This fact is well supported by different studies in which no patients were aware of any significant change in their vision but had retinopathy.[59]

Regarding the details of retinopathy which included retinal hemorrhages, cotton wool spots and macular edema, most of the patients (61.8%) developed cotton wool spots, 38.2% patients had retinal hemorrhages and none had macular edema. International data has also revealed cotton wool spots as the most frequent abnormal fundoscopic finding in these patients.[51,67]

Similar to previous studies, this study also showed that retinal changes usually develop within the first 12 weeks of INF treatment.[53] Therefore, there is sufficient evidence to point out the first 3 months as the most likely time for its development. The appearance of retinopathy later than 3 months after the start of therapy are unlikely due to it.[49,53,67,70]

Results of current study showed that cotton wool spots appeared in more patients within the first 6 weeks of therapy while retinal hemorrhages were more commonly seen in the following 6 weeks, strengthening further the fact already published in 200.[61]

Regarding the frequency of retinopathy by age, it was seen that retinopathy developed more frequently with advancing age. The mechanism of INF induced retinopathy is thought to be related to disturbance in retinal micro- circulation and atherosclerotic changes occurring more commonly in older age.[71]

CONCLUSION

It is concluded that INF induced retinopathy develops in considerable number of patients and is most commonly detected during the first 12 weeks of therapy. The most common retinal changes are cotton wool spots. Therefore, it is recommended that every patient on interferon therapy should have regular eye examination for surveillance of retinopathy to prevent blindness, a dreadful consequence.

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OUTCOME OF ULTRASOUND-GUIDED CORE NEEDLE BIOPSY OF VARIOUS BREAST LESIONS

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Abstract

Objective: To determine outcome of core needle biopsy in terms of its procedure, complications and histopathological findings and their correlation with radiological imaging using ultrasonography and mammography.

Design: Cross-sectional study

Place and Duration of Study: Department of Radiology, Avicenna Medical College & Hospital, Lahore. From January 2017 to June 2019.

Methods: Patients with suspected breast lesions were included in the study. Radiological imaging was done using ultrasonography and mammography. Lesions were classified using Breast Imaging Reporting and Data System (BIRADS) criteria. Core needle biopsy was performed under ultrasound imaging using a standardized technique. Tissues were sent for histopathological analysis. Lesions were characterized as benign if they were classified as BIRADS category 3 whereas they were classified as malignant if they were classified as BIRADS category 4 and 5. The results of BIRADS classification were compared with the histopathological analysis of the specimens obtained.

Results: A total of 152 patients were evaluated in this study. The mean age of the patients was 45.9 years ± 9.6 (range: 22 – 68) years. Positive family history of breast cancer was seen in 20.4% of the cases. Malignant lesions (BIRADS class 4 and 5) were seen in 67.1% of the cases and benign (BIRADS 3) in 32.9% cases. No major complication of CNB was noted except for a few cases of unbearable pain on needle insertion and hematoma formation in one case. Invasive ductal carcinoma was the commonest outcome on histopathology. The sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of core needle biopsy was calculated to be 94.6%, 100%, 100%, 87.0% and 96.1% respectively.

Conclusion: Ultrasound guided core needle biopsy is a very useful, minimally invasive technique to evaluate suspicious breast lesions. The method has high diagnostic accuracy, sensitivity and specificity. It does not carry any major side effects and can be performed in outpatient clinic.

Keywords: ultrasound guided, core needle biopsy, breast cancer, histopathology, BIRADS

Breast cancer is the commonest cancer prevalent in female population around the world with prevalence of about 25% in women aged 50 – 70 years.[1,2] In Asia, it constitutes 27.1% of all female malignancies and is considered to be the most frequent cancer seen in either male or female gender.[3,4] Core needle biopsy (CNB) under ultrasound imaging is taken as standard of care for the diagnosis of various breast pathologies, especially those that are non-palpable.[5] This procedure is safe, cost-effective and less invasive compared with surgical excision.

CNB is considered superior to fine needle

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aspiration cytology (FNAC) in various breast lesions and is the reason it is the preferred modality these days.[6] Treating physicians opt for CNB since it yields a significant breast tissue for analysis and confirmatory histopathological tissue diagnosis. CNB is usually preferred over FNAC when the diagnosis of breast lesions is suspicious and the lesion demands mandatory histopathological evaluation to reach a final tissue diagnosis.[7,8]

In our country, before the introduction of trucut biopsy or CNB, suspected malignant lesions of breast that were considered to be life threatening were subjected to surgical excisional procedures like mastectomy, excision biopsy, quadrantectomy, or wide local excision.[9] The excised tissue was then sent for pathological evaluation.

The aim of this study was to determine results of core needle biopsy regarding the technique, complications, histopathological findings and their correlation with the radiological imaging findings.

METHODOLOGY

A cross-sectional, descriptive study was conducted from January 2017 to June 2019 at the Department of Radiology, Avicenna Medical College and Hospital, Lahore, Pakistan. The study adhered to the principles of ethical medical practice as laid down in Declaration of Helsinki and was conducted after obtaining approval of its synopsis from the Ethical Review Board of the same institution. The ultrasound machine used for CNB was the GE Logiq P5 ultrasound machine with a linear probe of variable frequency ranging from 7.5 to 12 MHz. We also conducted mammography of our suspected patients from Department of Radiology, Shaikh Zayed Hospital, Lahore. Lesions were classified using Breast Imaging Reporting and Data System (BIRADS) criteria of the American College of Radiology based on the combination of mammography and/or ultrasound findings.[10] All biopsies were performed by one and the same radiologist (SbA and SA).

For obtaining tissue using CNB we employed following standard procedural technique. The patient was first imaged with ultrasound to see the site of the breast lesion. Afterwards, the skin of the area was disinfected using 5% povidone iodine solution and area draped with standard opsite tape. We injected 5ml of 1% lidocaine solution as local anesthetic in the area of interest. Under direct ultrasound imaging the CNB needle was injected at the site of lesion and 3-4 successive specimens were obtained. The depth of needle insertion into the lesion was constantly monitored using consecutive transverse and longitudinal images obtained on ultrasonography (Figure 1). The tissue specimens were fixed in formaldehyde and sent to Department of Pathology of Avicenna Medical College for histopathological analysis.

We recorded the data obtained in a pre-designed questionnaire. The study variables included age of the patient, personal or family history of breast cancer, clinical characteristics, location and size of the lesion and BIRADS classification. We also studied complications of the biopsy procedure and results of histopathological analysis.

Lesions were characterized as benign if they were classified as BIRADS category 3 whereas they were classified as malignant if they were classified as BIRADS category 4 and 5. The results of BIRADS classification were compared with the histopathological analysis of the specimens obtained.

The data were analyzed using the Statistical Package for Social Sciences (SPSS version 23.0, IBM Statistics, Chicago, IL, USA). Numerical data are presented as mean ± standard deviation (SD) whereas the categorical data are presented as frequencies and percentages. Following reliability indices were calculated for CNB and histopathology: true positive (TP), false positive (FP), sensitivity (SE), specificity (SP), positive predictive value (PPV), negative predictive value (NPV) and diagnostic accuracy (DA).

RESULTS

During the two and a half year period, 152 patients were evaluated in this study. The mean age of the patients was 45.9 years ± 9.6 (range: 22 – 68) years. Majority of the female patients belonged to

age groups 35 – 45 years and 45 – 55 years (table 1). Positive family history of breast cancer was observed in 20.4% of the cases. Lesions in the form of palpable masses were seen in 89.5% of the cases (Table 1).

Majority of our patients underwent combined investigation with both ultrasonography and mammography (85.5%). Lesions were categorized as probably malignant or malignant, BIRADS class 4 and 5 respectively, in 67.1% and probably benign (BIRADS 3) in 32.9% (table 1). Their mean size of the breast lesions was found to be 24.2 ± 7.3 mm on ultrasonography.

Table 2 summarizes results of the core needle biopsy procedure in the study population. We used BARD automatic gun in 79.6% of the cases (figure 2). The procedure was not very long and took less than 30 mins in most of the cases (92.1%). As far as complications of the procedure are concerned, we did not observe any major complications like hemorrhage or puncture site infection. However, minor complications like unbearable pain after the procedure were observed in a minority of the patients. One case of self-resolving hematoma was also observed.

Table 1: *Demographic, Clinical And Radiological Imaging Data of the Study Population*

Specifications	Number	Percentage
Age Range		
<35 years	21	13.8
35 - 45 years	54	35.6
45 - 55 years	55	36.2
55 - 65 years	14	9.2
>65 years	8	5.2
Family History of Breast Cancer		
Yes	31	20.4
No	121	79.6
Clinical Presentation		
Palpable mass	136	89.5
Non-palpable	16	10.5
Location of the lesion		
Right breast	72	47.4
Left breast	80	52.6
Imaging Technique		
Ultrasound	22	14.5
Combined ultrasound and mammography	130	85.5
BIRADS Classification Before Biopsy		
BIRADS 3	50	32.9
BIRADS 4	70	46.0
BIRADS 5	32	21.1

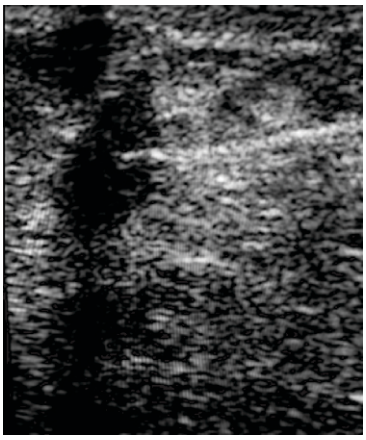

Figure 1: *Ultrasound Guided Core Needle Biopsy Image Showing Needle Inside the Breast Lesion*

Figure 2: *Automatic Core Needle Biopsy Gun with 14 G Needle*

One case with inconclusive report on histopathology underwent repeat CNB after an interval of one month. Histopathological analysis revealed invasive ductal carcinoma to be the commonest finding in our study population (55.9%) (table 2). Majority of our study cases underwent subsequent surgical excisions in the form of mastectomy, quadrantectomy or wide local excision. We also calculated diagnostic accuracy of BIRADS classification system considering histopathology as gold standard. The reliability indices are given in table 3. The sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of core needle biopsy was calculated to be 94.6%, 100%, 100%, 87.0% and 96.1% respectively (table 3).

DISCUSSION

The main objective of the study to determine outcome of core needle biopsy of various breast lesions was successfully met. We observed that majority of the lesions fell in the category of

Table 2: *Data On Core Needle Biopsy Procedure and Post-Biopsy Histological Finding*

Specifications	Number	Percentage
Type of materiel used for biopsy		
BARD automatic gun	121	79.6
Semi-automatic needle	31	20.4
Duration of the biopsy act		
Less than 30 minutes	140	92.1
More than 30 minutes	12	7.8
Complication		
Immediate complications	5	3.2
Late complications	7	4.t
Number of specimens		
3 specimens	50	32.9
4 specimens	80	52.6
6 specimens	22	14.5
Histology on ultrasound-guided biopsy specimens		
Adenofibroma	19	12.5
Fibro-cystic dysplasia	22	14.4
Invasive ductal carcinoma	85	55.9
In situ ductal carcinoma	6	4.0
Others*	20	13.2

Table 3: *Reliability Indices Radiological Imaging Before Core Needle Biopsy as Compared with Histopathology of Tissue Specimens*

Reliability Indices	Birads Before Biopsy (N = 152)	Histopathology After CNB (N = 152)
True Positive(TP)	106 (69.7)	113 (74.3%)
False Positive (FP)	0 (0.0%)	0 (0.0%)
False Negative (FN)	6 (3.95%)	3 (2.0%)
True Negative (TN)	40 (26.3%)	36 (23.7%)
Sensitivity (SE = TP/TP+FN)	94.6%	97.4%
Specificity (SP = TN/TN+FP)	100%	100%
Positive Predictive Value (PPV = TP/TP + FP)	100%	100%
Negative Predictive Value (NPV = TN/TN + FN)	87.0%	92.3%
Diagnostic Accuracy (DA= (TP + TN)/(FP + FN + TP + TN)	96.1%	98.0%

BIRADS 4 & 5 and proved to be invasive ductal carcinoma on histopathology. The outcome of CNB yielded very high precision and reliability on statistical analysis. We did not observe any major complication of CNB procedure, however, a few patients reported pain which was unbearable in the beginning but then controlled with oral or intramuscular analgesics.

CNB has been preferred over other interventional procedure owing to the fact that it yields very reasonable volume of the tissue which can be analyzed histopathologically and provide very useful details in reaching a confirmatory diagnosis of various breast pathologies.[11,12] Though we did not find any significant bleeding incident in our study. But previous reports have mentioned a significant association between using large bore CNB needles and hematoma formation at the site of procedure.[13] Incidence of bleeding during the procedure can be reduced by adequate application of local anesthesia so that the patient does not exert more during the procedure. Patients should be counselled in detail about the procedure to achieve good cooperation during the procedure. Excessive exertion and squeezing during the procedure can lead to benign but large hematomas which can resolve spontaneously gradually over time. A few of our cases experienced severe pain during the procedure which can be attributed to low pain threshold of the patient, insufficient local anesthesia or We attribute this pain to probable low pain threshold of the patient or insufficient local anesthetic application in these patients or potentially a psychosomatic reaction.[14]

In our study, report of single tissue sample came out to be inconclusive and we had to repeat the test for histopathology after an interval of one month. Earlier studies by Gukas et al. and Rikabi et al. reported inconclusive reports in 3.6% and 2.2% of their cases respectively.[15,16] The latter study reported that 83.3% of the inconclusive reports turned out to be malignant on trucut biopsy. Therefore, it is advisable that the lesions which yield inconclusive results should be sent for trucut biopsy to reach a definitive diagnosis.[17,18] Lastly, various studies have reported sensitivity of CNB between 88.9% - 98.1% and specificity of 91.3% - 100%.[8,19,20] The results of our study are in accordance with previous researches as we also observed very high reliability indices of CNB (table 3).

The major limitation of our study was its small sample size. We recommend larger studies with involving multiple centers to generate more national data on the subject. Secondly, we could not follow up the patients for longer period of time to see ultimate outcome of various breast lesions. Future studies are recommended with longer follow up so that regional data on outcome of various breast pathologies could be generated. Lastly, our histopathological evaluation relied most on the cellular classification of the tissues and did not use histochemistry markers to further characterize these breast lesions. We reco-

mmend use of various histochemical markers while studying breast pathologies in future studies.

CONCLUSION

Ultrasound guided CNB is a very useful technique in acquiring tissue samples for histopathological evaluation. The method has high diagnostic accuracy, sensitivity, specificity and PPV. We can prevent unnecessary surgeries by employing this technique in our routine breast oncological practice. There are no significant major adverse effects of this technique and patients generally tolerate it quite well.

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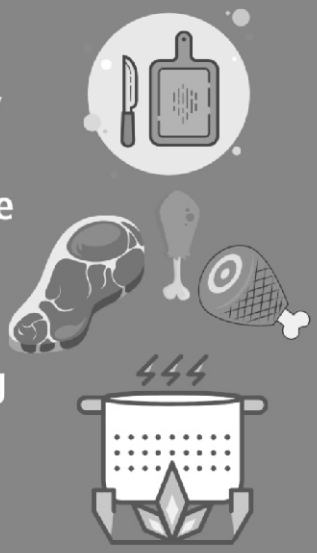
Practise food safety

Even in areas experiencing outbreaks, meat products can be safely consumed if these items are cooked thoroughly and properly handled during food preparation.



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