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A STITCH IN TIME SAVES NINE – ANALYTIC REVIEW OF 66 CASES OF CHEST TRAUMA

Ghulam Shabbir Pervez, Syed Saqib Raza Bokhari, Saima Sultan, Ahsen Nazeer Ahmad, Muhammad Mohsin Gillani, Ahmad Abutalib

Sharif Medical & Dental College. Lahore

Abstract

Human passion for speed and quarrels has contributed a lot to morbidity and mortality. Trauma stands amongst the major causes of death all over the globe. Amongst all variants of trauma chest trauma demands the maximum number of lives due to its severity. A study claims that 25% deaths are caused by thoracic trauma in USA. When we bring in to consideration the developing countries, the toll is considerably higher. A prompt evaluation and quick intervention can significantly reduce this number. We reviewed 66 patients who presented with chest trauma. In all of them a thoracotomy, whether open or Video Assisted, was performed after an initial Tube thoracostomy. These patients were operated during one year and follow-up made for a minimum of 3 months. Majority of them belonged to the age group 10-40 years with a predominance of males. 30 had blunt while 36 penetrating injuries. Haemo-pneumothorax was the most common presentation (46/ 66). 56 were managed by Video-assisted thoracotomy while the rest were offered a limited/ standard thoracotomy. The time interval between injury and thoracotomy was less than 72 hours in 56. A good outcome was achieved in 54 patients where lung was completely restored with no morbidity. All remained well in their follow-up visits with no complication regarding surgery.

It is concluded that early surgery in Thoracic Trauma in selective cases not only improves the outcome but reduces financial burden by decreasing hospital stay.

Key Words: Chest trauma, Video-assisted Thoracotomy, Haemo -pneumothorax

Human beings are in a habit of quarreling for different reasons since their creation. The first quarrel that has been narrated in religious books dates back to the beginning of humanity. The invention of the wheel added acceleration to human passion for speed, leading to an increase in the magnitude and intensity of trauma resulting in ever-growing morbidity and mortality. Trauma on the whole, remains the leading cause of death in young and bread-earning individuals. The American Association for Surgery of Trauma determined that 1.2 million people die in road traffic accidents in a year, 90 % of which belong to developing or under-developed countries[1]. This fact has got a significant impact on the social life as well as economy of these countries. The developing countries suffer more in this regard owing to the lack of health facilities as well as delayed transportation to treatment centers. Most of the patients received in hospitals have already lost the precious golden hour of the management of trauma. It is therefore essential that a prompt management should be initiated as soon as possible to these patients. Majority of these patients are sufferers of poly trauma. Although the medical education and training courses like BLS and ATLS have contributed a lot towards the development of patient care in trauma patients, yet, a lot has to be done. The newly developed diagnostic techniques and proficient anesthesia play a key role. An estimate by WHO reveals that nearly 5 million people die due to injury every year. This alarming situation can be effectively dealt with by increasing the awareness of trauma management in health professionals.

A large number of these patients suffer from Polytrauma with Thoracic trauma making a major component. Ludwig et al observed that approxi-

Correspondence: Ghulam Shabbir Pervez (Head of Thoracic Surgery Department Sharif Medical and Dental College.)
Email: ghulamshabbirpervez@gmail.com

mately 2/3rd of the Polytrauma patients have chest trauma[2]. It has also been observed that there are nearly 17000 deaths due to trauma with nearly 25% of these directly attributed to thoracic injury[3]. Chest trauma can be penetrating or blunt. Although penetrating has a higher morbidity / mortality, yet fortunately 90% incidents are of blunt. Nevertheless, chest trauma stands 2nd highest in mortality after head injury[2]. Waydhas C. found that mortality was reported to dramatically increase in patients with thoracic trauma[4]. Thoracic injuries are not only responsible for early mortality, but they have a definite role in late deaths. This is because of the fact that thoracic injuries cause not only excessive haemorrhage but also injury to the lung. Lung injuries contribute to the development of Multi Organ Failure and therefore represent major cause of late death[5]. Regardless of the type of chest trauma, prompt evaluation and management decision making is required to deal with it successfully. Anything starting from a simple tube thoracostomy and ending up with emergency thoracotomy may be needed. The pivot of management stands quick awareness of the full extent of injuries. Gage A and colleagues suggest that blunt chest trauma should be managed by strong analgesics, fixation by surgical techniques, chest physiotherapy and respiratory care along with mobilization of the patient as early as possible[6]. Most workers believe that early measures to deal with thoracic trauma include Tube thoracostomy, pain control, pulmonary toilet and observation. 85 - 90 % patients can be managed with these measures[7]. However, trauma causing major bleeding and organ damage requires further intervention. In such situations one needs a complete assessment of the structures within the chest cage. At times one can come across confusing situations like diaphragmatic injury simulating a pneumothorax. Tube thoracostomy being a somewhat blind procedure, chances of piercing the stomach in suspicion of a pneumothorax after diaphragmatic injury are not so uncommon. Thoracotomy being an aggressive option is usually avoided unless required urgently. Video-assisted entry to the thoracic cage is no doubt a very useful alternative. Michael Goodman and colleagues stated that Video-assisted Thoracoscopy (VATS) has been used in the management of thoracic trauma for indications such as retained haemothorax, persistent air leak, empyema and evaluation of diaphragmatic and mediastinal injuries[8]. VATS is more frequently required to manage penetrating chest trauma due to reasons well known. Milanchi and colleagues recommend use of VATS even under local anesthesia and reproduced that a thoracotomy was avoided in 44% patients based on the findings of Thoracoscopy[9]. Use of VATS has successfully replaced thoracotomy in a significant number of cases. It has the merits of shorter operative time, non-blind area, exact surgical path and less bleeding[10]. Use of VATS is not limited; this highly reliable and effective procedure is very well tolerated by majority of patients and it can successfully diagnose and deal with lung injuries and rib fractures[11,12]. The procedure also has the edge that it is a little more aggressive as compared to tube thoracostomy[11]. These facts support its use in both variants of chest trauma. While there is almost a consensus on frequent use of VATS in chest trauma, slight controversy prevails in the selection of time for VATS. Some people recommend its use within 24 hours while others would delay it for 72 hours[13, 14]. Use of VATS can replace tube thoracostomy wherever indicated. No matter at what time its application is selected, VATS has definitely changed the prognosis of trauma sufferers.

METHODS

This cross-sectional study was conducted in two tertiary care hospitals from January – December 2017. Both the hospitals are affiliated to medical colleges. 66 Patients with thoracic trauma who underwent operative management in the form of VATS or open thoracotomy regardless of age and gender discrimination were included. Patients of both blunt and penetrating trauma were included. General or regional anesthesia both were utilized as per requirement of the situation. Post operative

follow up was done for 3 months. Outcomes of surgical management were evaluated in terms of post operative lung expansion, duration of chest drain and need for any other surgical intervention after the primary surgery. Informed consent was taken in all cases and surgery was performed as per patient's desire.

RESULTS

A total of 66 patients were included in the study. All of them presented with a history of trauma in Emergency department of either of the 2 hospitals. After primary survey, it was found that they needed surgical intervention. Initially Tube thoracostomy was done in most of the patients. However in some of them tube thoracostomy was done in some other hospital and then they were referred to our hospitals. Trauma, as we know, is not confined to age or sex. We received patients of all ages. Table 1 shows the age distribution in our patients. Larger number of these patients was more than 10 and less than 40 years.

Table 1: *Age Distribution*

Age in years	No. of patients	Percentage of patients
< 10	6	9.1%
10 – 20	10	15.1%
20-30	16	24.2%
30-40	22	33.3%
>40	12	18.2%

Following is the gender distribution in our patients.

Table 2: *Gender Distribution*

MALE	45	45%
FEMALE	21	55%

Type of Trauma:

The pattern of trauma was almost equal in both types as shown in the table below.

Penetrating injuries, however, are split into missile and sharp injuries depending upon their nature.

Table 3:

Type of Trauma	No. of Patients		
Blunt	30		
Penetrating	36	Missile injuries	4
		Sharp injuries	32

Variations of injury:

Table 4 presents the variation of presenting problem in these patients.

Table 4:

Problem at presentation	Number of Patients
Pneumothorax with lung injury	8
Haemo-pneumothorax with or without Rib fracture	44
Diaphragmatic Injury	12
Cardiac Injury	2

Indications for surgical intervention are shown in Table 5.

Table 5:

Indication	Number of Patients
Massive/ Clotted / Loculated Haemothorax	21
Pneumothorax with BP Fistula	22
Pyo-pneumothorax	9
Diaphragmatic Tear	12
Cardiac Injury	2

Table 6: *Time Duration between Injury & Surgery*

Time duration	No. of patients	Percentage of patients
<24 hours	11	16.6%
24-72 hours	45	68.2%
>72 hours	10	15.2%

Table 7: *The Choice of Procedure Adopted*

Procedure	No. of patients	Percentage of patients
VATS	56	85%
Limited / Standard Thoracotomy	10	15%

Outcome of surgery was evaluated as Good, Satisfactory and poor according to criteria mentioned below

- Good indicates that we achieved to have a fully expanded lung with no or negligible volume loss on chest x-ray and chest drains removed

maximum with in a week's duration.

- Satisfactory where more than 80% lung expansion achieved but patient had to be sent home with a chest drain for a leak.
- Poor where we couldn't achieve an expansion more than 60% and further surgical measures were advised.

The outcome of patients is presented below on the basis of criteria mentioned.

Table 8:

Outcome	No. of patients	Percentage of patients
Good	54	82%
Satisfactory	10	15%
Poor	2	3%

All the patients were followed up for at least 3 months postoperative and were in satisfactory state of health.

DISCUSSION

Trauma is perhaps the most significant killer in human beings. The intensity of the problem is similar for both developed and developing countries. Whereas the developing countries face the threat due to lack of facilities, the developed world faces the consequences of development. Faster traveling modes and sophisticated weapons are examples of that. An estimated figure of 1.2 million annual deaths due to trauma[1] clearly defines the severity of the issue. One should not be surprised to know that 90% of these deaths take place in developing countries, the principal reason behind it being lack of transport and health facilities. The Golden first hour after trauma is usually wasted in developing countries. So it's essential that a quick management protocol must be followed in tertiary care hospitals. The need for quick response is much more enhanced in patients having chest trauma. Lungs being more vulnerable to infections lead to Multi Organ Failure ultimately resulting in death[5], thus chest injuries need to be managed more quickly. Both the hospitals where the study was conducted are fortunately near highways and that made our job more convenient.

Chest Trauma is potentially life threatening because of the associated complications. A wide range of complications is attributed to Thoracic Trauma. Ronald and colleagues determined that respiratory failure, pneumonia and pleural sepsis are the most common complications[15]. While the first two require medical treatment, Pleural sepsis can be accurately managed by adding surgery. Clotted haemothoraces are not only difficult to be drained with simple tube thoracostomy but also play an important role in pleural sepsis. Major surgical intervention was thought to be too aggressive in the past so it was denied in most of the patients. Evolution of VATS along with safer anaesthesia techniques has provided a sigh of relief for these patients. Following guidelines by Chou et al[11] we utilized VATS in majority of these cases (85%). Patients who directly came to our Emergency departments were given the option of Tube Thoracostomy or VATS and those who opted for VATS were operated after getting baseline workup. So the majority of them were operated within 72 hours of injury (56/66). Early surgical intervention is recommended by most people. We tried to keep this interval as short as possible following Gabal and H. Sing[13,14]. VATS was applied as a standard procedure in most of the patients. This is also well documented in most of the studies[9,10,11, and 12]. However in 12 patients VATS incision had to be extended to a limited thoracotomy because of uncontrollable bleeding, air-leak or diaphragmatic injury. An initial thoracotomy incision was made in patients with missile injuries or those who were referred to us by other hospitals where an initial Tube Thoracostomy remained unsuccessful. Patients with suspected cardiac injury were also kept in this category.

Although the literature quotes more incidence of blunt trauma as presenting mode of injury[2], in our study 55% patients are of penetrating trauma. It pertains to high incidence of interpersonal conflicts in our society and use of weapons in minor conflicts. Also the inclusion of patients of stab wounds of upper abdomen causing diaphragmatic injury shif-

ted the injuries towards penetrating injuries. In a study by Biplah Mishra, 21 cases of cardiac injury were reported over a period of 5 years[16]. Our study includes 2 cases of cardiac injury. One of these patients had a self-inflicted gunshot where the bullet lodged in the lower lobe of lung after creating a partial rent in right ventricle. The other one was a stab wound causing tear in pericardium and cardiac muscles. Both patients survived due to early intervention (open thoracotomy).

The outcomes of surgical intervention in trauma are assessed by duration of hospital stay and cessation of drainage in chest tube. In the literature, hospital stay after VATS ranges between 5-12 days[9,17]. In our study, 82% patients had a good outcome as the lung expanded within a week, chest tube was removed and the patient discharged home. In a study by Milanchi, hospital stay was reported to be 12 days [9].

CONCLUSION

Chest trauma being the major component in Polytrauma patients needs early thoracic surgical intervention. VATS has promising results and must be employed in the management of thoracic trauma patients.

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ANTIMICROBIAL RESISTANCE PATTERN OF CLINICAL ISOLATES OF INFECTED WOUNDS

[1]Khalil ur Rehman, [2]Faizan Rasool , [3]Anas Rafiq , [4]Saima Anwar
[5]Rafiq Ahmad Shahid, [6]Aasim Tahir, [7]Muhammad Asif

[1]Professor of Pathology, Abwa Medical College, [2]King Edward Medical University, Lahore,
[3]The Park Lane Clinic, Lahore, [4]King Edward Medical University, Lahore
[5] PGMI/Ameer-ud-din Medical College, Lahore, [6]Technologist Indus Hospital, Lahore
[7]King Edward Medical University, Lahore

Abstract

The progressively increasing invasive systemic infections are among the lead health problems caused by the wound infections. The morbidity and mortality rate is increased due to the widespread use of antibiotics and resistance caused by the microorganisms.

AIMS & OBJECTIVES: The aim of study is to isolate the causative organisms and study their pattern of drug susceptibility of bacteria cultured from superficial wound infections.

METHODOLOGY: Analytical cross-sectional study was conducted at King Edward Medical University. A total of 87 patients were selected who had superficial wound infection. Sterile cotton swabs were used to obtain the specimens from wounds and processed. Bacterial isolation done by culturing technique and susceptibility testing were performed. Identification of organisms was done by biomedical tests. Kirby-Baur disc diffusion method was used for sensitivity testing.

RESULTS: Eighty-seven patients having wound infection were selected for sample collection. Gram positive isolate were 43 (49.5%) and gram negative were 44 (50.5%). Forty two out of 87 (48.2%) isolated organisms were S. aureus, Pseudomonas aeroginosa (19.5%), E.coli (13.7%), Enterobacter (8.04%), Acinetobacter (5.7%) and Klebsiella (2.2%). Ninety-three per cent of gram positive isolates showed resistance to trimethoprim-sulpha methoxazoal followed by 83.7% to penicillin, 72.1% to erythromycin and 2.3% resistance to linezolid. None of isolate exhibited resistance against vancomycin. Out of gram negative isolates, 97.7% were resistant to ceftriaxone followed by 93.1% to cefotaxime, and only 11.3% to imipenum.

CONCLUSION: Isolation of S. aureus were dominant among the both gram positive and gram negative broad spectrum bacteria. Most of them showed resistance to different tested antibiotics. In vitro testing for sensitivity was less effective by ampicillin, ceftriaxone, penicillin and trimethoprim-sulphamethoxazole. The greater effectiveness was shown by many antibiotics such as gentamicin, imepenum, linezolid, amikacin and vancomycin.

The progressively increases invasive systemic infections are among the lead health problems caused by the wound infections. Wide range of microorganisms may cause wound infections including bacteria (aerobes and anaerobes), fungi and parasites. Bacteria are a predominant cause of wound infections.[(1)] Gram positive and gram negative bacteria both cause wound infection. In most studies high bacterial isolation rate >70% have been reported as Staphylococcus aureus, Pseudomonas aeurginosa and bacteria belonging to family Enterobacteriacea.[(2)]

Wound infection can lead to inhibition of the healing process that results in complication in treatment and management. Such Patients require prolonged hospitalization and in some cases wound infection may cause high morbidity and mortality.[(3)] Frequent use of inappropriate antibiotics prescribed in wound infection is the most common cause of increase pathogenic bacterial resistant strains[(4)]. The

purpose of this study is to find the current prevalence and distribution of bacterial infections in the local population. This study gives a view about the sensitivity and resistance pattern of isolates. It will help to understand the ongoing crisis and will provide outline about choice of treatment.

METHODOLOGY

Pus /wound swab samples were collected from 87 patients of Mayo Hospital, Lahore with complaints of discharge, painful delayed and non-healing wound infection. Aseptic technique was used to collect the samples with swab from surface exudates of open wounds. Moist sterile gauze and sterile normal saline were used to wash-off the contaminants.

After removing the dressing, the sterile normal saline was used to decontaminate the wound. Sterile cotton swabs were used to collect the specimen with sufficient pressure and rotation. The inner surface of wound was swabbed gently and samples were sent to laboratory for culture, further identification and susceptibility testing. The transportation was done by using Amies transport media to laboratory.

In the microbiology laboratory, samples were processed in biological safety hood. Routine culture plates including Chocolate agar, Blood agar and MacConkey plates were used to isolate the organisms. The specimens were inoculated through quadrant streaking method to get pure growth. These plates were incubated at 37 for 24 hours. A 0.5 McFarland suspension was prepared from the isolated colony and speeded through lawning method on Müller-Hinton agar plates. Appropriate antibiotic disc were applied on culture plate and incubated at 37°C for 18 hours. After incubation zone of inhibition measured according to CLIC 2017.

DATA ANALYSIS PROCEDURE

The statistical package for social science (SPSS) version 21 was used to enter and analyze the data. The mean ± SD was used as quantitative variables like age. The gender as qualitative variable was presented with frequency and percentages.

Ninety-five per cent confidence levels were used to evaluate and $P< 0.05$ was considered statistically significant. The frequencies and mean were used for descriptive analysis and tables and charts used for the presentation of data results.

RESULTS

A total of 87 wound swab samples from patients of different ages and sex were included in this study. The male and female ratio was 1:1.3, 49 (56.3%) were male whereas 38 (43.6%) were female. A total of 87 bacterial isolates were obtained, 43 (49.4%) were gram positive while 44 (50.5%) were gram negative bacteria. S. aureus showed predominance with 43 (49.4%), followed by Pseudomonas aeruginosa 17(19.5%), E. coli 12 (13.7%), Enterobacter 7 (8.04%), Acinetobacter 5 (5.7%) and Klebsiella spp. 2 (2.2%) (Fig.1)

Seven antibiotics were slected to test the gram positive isolates . The organisms showed variation in their patterns of susceptibility to all the antibiotics used. Gram positive isolates were sensitive to a higher extent to gentamicin (86.4%). Maximum number of isolates were resistant to trimethoprim-sulphamethoxazole followed by penicillin G (83.7 %), clindamycin (69.7%), erythromycin (72.1%) and least resistant to linezolid (2.3%) illustrated in (Fig. 2).

Gram negative bacteria (n=44) were tested against seven selected antibiotics. The isolates showed resistance to ceftriaxone in 97.7% cases including cefotaxime (93.1%), Augmentin (88.6%) and at minimum extent to imipenum (11.3%). Susceptibility pattern of all gram negative isolates is shown by simple bar graph in (Figure.3)

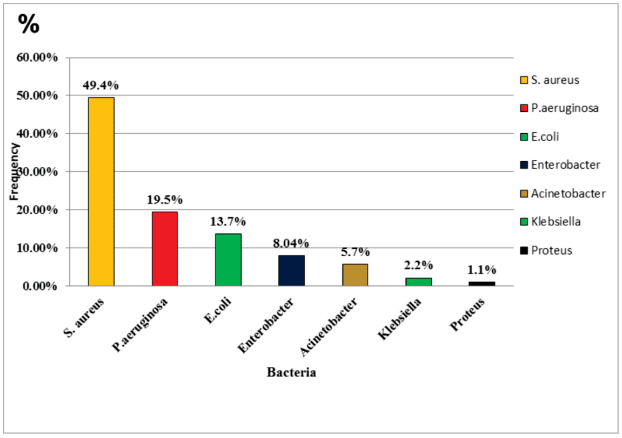

Fig. 1: *Frequency of bacteria isolation from infected wounds*

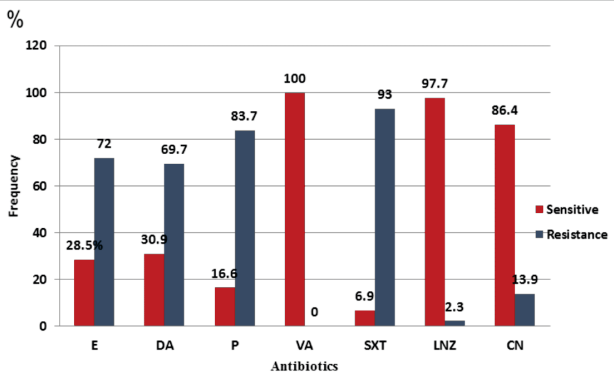

Fig. 2: *Susceptibility pattern of Gram positive bacteria*

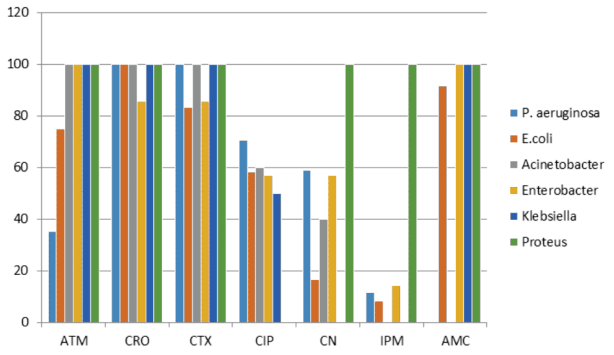

Fig. 3: *Susceptibility pattern of Gram negative bacteria*

CN: Gentamicin, SXT: Trimethoprim-sulphamethoxazole, P: Penicillin G, E:Erythromycin, LNZ: Linezolid, IMP: Imipenum, VA: Vancomycin, DA:Clindamycin, CRO: Ceftriaxone, CTX: Cefotaxime, ATM: Augmentin, CIP: Ciprofloxacin

DISCUSSION

The mortality and morbidity rate is significant among the patients with wound infection and invoke substantial costs in hospitals. The complication in wound infection, costs of associated procedures and treatment goes on increasing due to antimicrobial resistance developed in wound pathogens.[5] Identification of pathogens and determination of their susceptibility pattern from clinical specimens is useful to improve patient care and chemotherapy selection.[6]

In the present study the male patients were more than females. This correlate with many studies done in different locations in Pakistan and other countries.[7] The explanation of male dominance in wound infection is due to their exposure to trauma because of their work such as industry workers, construction employees, transporters and farmers.[8]

The studies that indicate the predominance of S. aureus and E. coli in the wound isolates was reported in Ethiopia and other parts of world[9]. The endogenous source of infection such as nose may be the cause of high prevalence of S. aureus in wound infections. The contamination from equipment for example surgical instruments is one of the reasons of this organism to cause infection.[10] Due to common distribution of S. aureus, as normal flora of skin the bacterium has easy access to enter in wound when the skin ruptures. S. aureus, has a higher rate of resistance to selected antimicrobial medicine.[9] An Indian study has shown similar results.[11]

In the present study, the gentamicin, vancomycin and linezolid showed higher sensitivity to same isolates. A study from Ethiopia reported similar results with 100% sensitivity patterns to vancomycin and gentamicin from the clinical isolate of Staphylococci.[11] The cost, less availability and toxic effects are the main reasons of remarkable susceptibility of gram positive bacteria to vancomycin and aminoglycosides (gentamicin) due to less prescription and use of these drugs.

All of the E.coli isolates described in present study were resistant to ceftriaxone and gentamicin.

For nosocomial infection, the reduction in sensitivity of antibiotics for E.coli suggests importance in clinical settings. Absolute resistance to ceftriaxone was noted for K. pneumoniae. The sensitivity of gentamicin was noted. This is comparable with results of previous studies from different countries. The ampicillin and chloramphenicol were resistant to most of gram negative isolates. The long time use and oral administration of these antibiotics affect absorption and cause resistant drugs patterns. The over and increasing use of some drugs as prophylaxis in patients also contribute in resistance to organisms.[12]

The commonly used antibiotics such as ceftriaxone, cefotaxim were less sensitive to P. aeruginosa whereas it showed high sensitivity to imipenum, gentamicin, and ciprofloxacin respectively in present study. For treatment of P. aeruginosa infections, the most effective drug used is oral Ciprofloxacin. This report is in agreement with the study conducted in Afghanistan.[13]

In present study, imipenem followed by gentamicin and ciprofloxacin were sensitive to Acinetobacter. The maximum resistance was seen against ceftriazone, cefotaxim, aztreonam and trimethoprim-sulphamethoxazol about (98%) same case was seen in a medical literature.[14]

In conclusion it can clearly be seen that most effective drugs against gram negative isolates were gentamicin, imipenum and ciprofloxacin whereas for gram positive isolates vancomycin and linezolid are the effective drugs. The limitation in the study is we could not elaborate the etiology of wound infections due to unavailability of clinical data. The number of antimicrobials was also limited in some isolates.

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ASSOCIATION OF HYPOVITAMINOSIS D WITH PRETERM DELIVERY IN FEMALES PRESENTING FOR DELIVERY IN TERTIARY CARE HOSPITAL

Aiesha Iftikhar Shah[1], Sunbal Khalid[2], Sumaira Fatima Sabir[1]

[1]Department of Obstetrics &Gynecology Lahore General Hospital Lahore,
[2]Department of Obstetrics & Gynecology, King Edward Medical University/ Lady Aitchison Hospital, Lahore.

Abstract

Introduction: Maternal vitamin D deficiency, as indicated by low circulating 25-hydroxyvitamin D [25(OH)D] levels, is common during pregnancy and is considered an important global public health problem.

Objective: To measure the association between hypovitaminosis D with preterm delivery in females presenting for normal delivery in a tertiary care hospital

Material & Methods: This case control study was conducted in Unit V, Department of Obstetrics and Gynecology, Lady Aitchison hospital Lahore from July to December 2017. Total of 630 cases (315 cases in each group) were included by non-probability, purposive sampling. Females of age 20-40 years with parity<6 presenting for delivery with labour pains (>10 pains in 30 minutes), cervical opening >3cm were included. Informed consent was obtained and patient demographic information was recorded. Females were divided in two groups (cases and controls) and underwent delivery. Blood samples were obtained and Hypovitaminosis D was labeled as serum vitamin D level <50nmol/l. Data was entered and analysis through SPSS 22. Odds Ratio was calculated to measure the association between hypovitaminosis D and preterm delivery. OR>1 was considered as risk for preterm delivery and was taken as significant.

Results: Mean age of women who had preterm and term delivery was 30.22±5.88 and 29.40±5.74 years. Mean vitamin D level in women with preterm and term delivery was 67.01±26.56 and 89.75±34.71. Women who had hypovitaminosis among them 124(72.5%) women had preterm and 47(27.5%) women had term delivery. Statistically significant association was seen between hypovitaminosis and mode of delivery. Odds ratio 0f 3.70 showed that women who had hypovitaminosis they had significantly 3.70 times more chances of preterm delivery as compared to that of women who did not have hypovitaminosis.

Conclusion: There is strong association and high risk for women with hypovitaminosis D and preterm delivery.

Key words: Association, Hypovitaminosis D, Preterm delivery, Normal delivery

Vitamin D has multiple functions that are critical in growth and development.[1] The best marker of vitamin D status is the circulating concentration of its metabolite 25- hydroxyvitamin D [25(OH)D]. When serum 25(OH)D concentrations have been measured in cohorts of pregnant women in the USA, many women from various ethnic groups living at different latitudes are found to have a low vitamin D status, regardless of the exact definition used.[2] A high prevalence of maternal vitamin D inadequacy during pregnancy and at delivery has been demonstrated in various ethnic populations living at different latitudes. A lack of vitamin D during pregnancy results in poor fetal and infant bone mineralization that may persist into later life. Also, low maternal vitamin D has been associated with an increased risk of lower birth weight, type 1 diabetes and asthma in the offspring. Low maternal vitamin D has also been associated with an increased risk of pre-eclampsia,[1]

Correspondence: Dr. Sumaira Fatima Sabir Senior Registrar Lahore General Hospital Lahore

Infants born at preterm are at higher risk than more mature infants for low 25(OH)D levels. Fur-ther investigation of the relationships between low 25(OH)D levels and preterm birth and its sequelae is thus warranted.[3] Baker, et al., in 2010; conducted a case control study and found that the prevalence of hypovitaminosis D among females undergoing preterm labour was 19% which was significantly higher than females undergoing delivery at term (11%, p-value<0.01).4 But after that in another study Baker, et al., found that the prevalence of hypo-vitaminosis D among females undergoing preterm labour was 7.5% which was slightly higher than females undergoing delivery at term (6.7%), how-ever, the difference was insignificant (p-value= 0.90).[5]

Rationale of this study is to measure the asso-ciation between hypovitaminosis D with preterm delivery in females presenting for normal delivery in a tertiary care hospital. In above mentioned articles, it was noticed that different studies have contradic-tion. On the basis of above mentioned contradictory evidences, we are unable to say whether hypovita-minosis D may be cause of preterm delivery. Through this study we want to assess that whether hypovitaminosis D is a risk and cause of preterm delivery, so that in future hypovitaminosis D can be cured at initial stages and risk of preterm birth can be prevented. The objective of this study was to mea-sure the association between hypovitaminosis D with preterm delivery in females presenting for normal delivery in a tertiary care hospital. We hypothesized that there is an association between hypovitaminosis D with preterm delivery in females presenting for normal delivery in a tertiary care hospital.

MATERIALS AND METHODS

This case control study was conducted in Unit V, Department of Obstetrics and Gynecology, Lady Aitchison hospital Lahore from July to December 2017. After approval from ethical committee, a total of 630 cases; (315 cases in each group was calculated with 80% power of test, 5% level of significance and prevalence of hypovitaminosis D = 19% in preterm and 11% in term delivery in females presenting in a tertiary care hospital) were included by non-proba-bility, purposive sampling. Females of age 20-40 years with parity<6 presenting for delivery with labour pains (>10 pains in 30 minutes), cervical opening >3cm were included. Females undergoing preterm delivery (gestational age < 37weeks on ultrasound) were taken as cases while Females undergoing term delivery (gestational age >37weeks on ultrasound) were taken as controls. Preterm delivery was defined as delivery of fetus before completed 37 weeks of gestational according to ultrasonography and last menstrual period dates. Hypovitaminosis D was labeled as serum vitamin D level <50nmol/l at the time of delivery. Multiple pregnancy (on ultrasound), Non-cephalic or malpre-sentation (on Ultrasound), Fetus having congenital anomalies (on ultrasound), Females with PIH (BP>140/90mmHg), DM (GTT>40mg/dl), preeclampsia (PIH with +1 protein urea on dipstick method) or eclampsia (convulsions) were excluded. Informed consent was obtained and patient demo-graphic information (name, age, gestational age, contact) was recorded. Females were divided in two groups, cases and controls as mentioned in inclusion criteria. Then females underwent delivery. Blood samples were obtained and were sent to the labora-tory of the hospital. Reports were assessed for vitamin D level. Hypovitaminosis D was labeled (as per operational definition). All this information was recorded on proforma.

Data was entered and analysis through SPSS 22. Quantitative variable like age, gestational age was calculated by mean standard deviation. Qualita-tive variable like parity and hypovitaminosis D was presented as frequency and percentage. Odds Ratio was calculated to measure the association between hypovitaminosis D and preterm delivery. OR>1 was considered as risk for preterm delivery and was taken as significant.

RESULTS

Mean age of women who had preterm and term

delivery was 30.22±5.88 and 29.40±5.74 years. In both groups minimum and maximum age of women was 20 and 40 years. The gravid status of women in preterm group was as follows: 55(17.5%) women had G-1, 106(33.7%) women with G-2, 69(21.9%) women with G-3, 47(14.9%) women with G-4 and 38(12.1%) women with G-5. In women with term delivery the gravid status was as follows: 63(20%) women had G-1, 110(34.9%) women with G-2, 66(21.0%) women with G-3, 45(14.3%) women with G-4 and 31(9.8%) women with G-5. (Table-1)

Women with preterm delivery their mean gestational age was 35.40±1.12 weeks and among women who had term delivery their mean gestational age was 39.02±0.82 weeks. Mean vitamin D level in women with preterm and term delivery was 67.01±26.56 and 89.75±34.71. In preterm group women minimum and maximum vitamin D level was 30 and 120 while in term group it was 30 and 150 respectively.

In preterm group there were 124(19.68%) women suffered from hypovitaminosis and in term group only 47(7.46%) women had hypovitaminosis. Women who had hypovitaminosis among them 124(72.5%) women had preterm and 47(27.5%) women had term delivery. As per p-value statistically significant association was seen between hypovitaminosis and mode of delivery. Odds ratio of 3.70 showed that women who had hypovitaminosis they had significantly 3.70 times more chances of preterm delivery as compared to that of women who did not have hypovitaminosis. (Table-2)

Table 1: *Gravid Status of Women (n=630)*

Gravida	Preterm		Term	
1	55	17.5%	63	20.0%
2	106	33.7%	110	34.9%
3	69	21.9%	66	21.0%
4	47	14.9%	45	14.3%
5	38	12.1%	31	9.8%
Total	315		315	

Table 2: *Association of Hypovitaminosis D with Preterm Delivery (n=630)*

Delivery	Hypovitaminosis D		Total
	Yes	No	
Preterm	124(72.5%)	191(41.6%)	***315***
Term	47(27.5%)	268(58.4%)	***315***
Total	**171**	**459**	***630***

Chi-Square Test= 47.59
p-value= 0.000
Odds Ratio= 3.70 (2.52-5.43)

DISCUSSION

In our study, it was observed that women who had preterm delivery among them mean vitamin D level was low as compared to that of women who delivered at term. i.e. Preterm delivery (Vitamin D level): 67.01 vs. term delivery (Vitamin D level): 89.75. There were total 171 women who had hypovitaminosis. Among these women 124(72.5%) had preterm delivery and 47(27.5%) women had term delivery. In terms of p-value a statistically significant association was seen between hypovitaminosis and preterm delivery. Odds ratio of 3.70 shows that women who had hypovitaminosis among them risk of preterm delivery is 3.70 times more s compared to the women who had normal vitamin D level. Shu-Qin Wei in his systematic review and meta analysis reported that low maternal vitamin D levels [25(OH) D550 nmol/l] may be associated with an increased risk of preeclampsia, GDM, preterm birth and SGA. Women with circulating 25-hydroxyvitamin D [25(OH)D] level less than 50 nmol/l in pregnancy experienced an increased risk of 1.58 for preterm birth.[6] Odds ratio for preterm delivery among women who had hypovitaminosis was high as compared to that of Shu-Qin Wei in his meta analysis. But this difference may be due to the difference analysis, as in meta analysis pooled analysis was done. Baker, et al., in 2010; conducted a case control study and found that the prevalence of hypovitaminosis D among females undergoing preterm labour was 19% which was significantly higher than females undergoing delivery at term (11%, p-value <0.01).[7] However in this study frequency of hypovitaminosis among women who had preterm deli-

very was 39.36% as compared to the women who had term delivery. i.e. 14.92%. In this study the frequency of hypovitaminosis was twice the frequency reported by Baker,et al in his study.

Arthur M. Baker in 2011; reported that the prevalence of first-trimester maternal vitamin D deficiency [25(OH)D <50 nmol/L] was comparable among women who subsequently delivered preterm compared with controls (7.5% versus 6.7%, p-value = 0.90).8 Results reported by Arthur M. Baker contradict the results obtained in this study. As Arthur M. Baker showed no significant difference for preterm delivery among women who subsequently delivered preterm compared with controls. JM Thorp in his study reported that Serum 25(OH)D concentration was not significantly associated with preterm birth (OR 1.33; 95% CI 0.48–3.70 for lowest versus highest quartiles).2 AW Shand in his study showed that there was no difference in the rates of pre-eclampsia, gestational hypertension, preterm birth or composite adverse pregnancy outcomes by 25OHD concentration.[9] i.e. Preterm Birth: Serum 25OHD concentration <37.5: 18(31.0%) OR(0.97), Serum 25OHD concentration <50: 33(56.9%) OR (1.02) & Serum 25OHD concentration <75: 46 (79.3) OR (0.79). JM Thorp and AW Shand results also contradict the results of this study. Both these studies showed no impact of hypovitaminosis for preterm delivery. But JM Thorp considered recurrent preterm birth which makes the design of the study different from that of this study. But somehow the results can be comparable for hypovitaminosis in relation to preterm birth.

CONCLUSION

Results of this study showed a strong association and high risk for women with hypovitaminosis D and preterm delivery. Further longitudinal studies are needed to establish the strong link between hypovitaminosis D and preterm birth. However for the time being it is very important that gynecologists should consider vitamin D status as essential marker like other routine screening parameters for women during pregnancy for the prevention of adverse pregnancy outcomes.

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Conflict of interest

The authors declare that there is no conflict of interests.

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SKIN ADNEXAL TUMORS- AN INSTITUTIONAL STUDY OF CLINICOPATHOLOGICAL FEATURES

Tabish S,[1] Mazhar S,[2] Afsar M,[3] Imran E,[4] Ashraf A,[5] Anwar A[6]

Department of Pathology, AIMC, Lahore, Department of Pathology, Allama Iqbal Medical College Lahore, Ex House officer, JHL,Lahore, MBBS Student, CMH, Lahore, Professor, Department of Pathology, AIMC, Lahore, Professor, Department of Pathology, AIMC, Lahore

Abstract

Background: Skin adnexal tumors are a large and complex group of benign and malignant neoplasms that express morphological differentiation towards pilosebaceous, eccrine and apocrine epithelia of skin adnexa. It is important to accurately diagnose skin adnexal tumors because some of them are part of syndromes associated with internal malignancy. However, these tumors are not commonly encountered in pathology practice.This study is, therefore, carried out to study clinicopathological features of these tumors in our setup.

Materials and methods: It was a cross-sectional study carried out at Department of Pathology, AIMC, Lahore from 15th April 2016 to 14th April 2017. Relevant biographic data was obtained from departmental record. H & E stained slides of all cases were examined. PAS staining was used where necessary.

Results: Twenty-four cases of skin adnexal tumors were diagnosed in a period of one year making 0.3% of total surgical specimens received. Male: Female ratio was 1:2. Head and neck was the most commonly involved site (79.16%). Majority of the tumors were benign (83.33%). Tumors of sweat gland origin were the commonest (50%). Proportion of malignancy was the highest for those of sebaceous origin.

Conclusion: Frequency of skin adnexal tumors is quite low. Tumors of sweat gland origin are the commonest among the group. Head and neck region is most commonly involved. Females are affected more than males. Benign tumors are typically seen in adults and middle age while malignant tumors in middle to older age group. Eccrine acrospiroma & pilomatixoma are the most common tumors. Tumors with sebaceous differentiation have highest risk of being malignant.

Skin adnexal tumors are a large and complex group of benign and malignant neoplasms that express morphological differentiation towards pilosebaceous, eccrine and apocrine epithelia of skin adnexa[1,2,3]. Most of the skin adnexal tumors are benign and complete surgical excision with clear margin is curative. Every benign adnexal tumor has a malignant counterpart, that is locally aggressive and may show nodal metastasis.[2,4] It is important to accurately diagnose skin adnexal tumor because some of them are part of syndromes associated with internal malignancy such as trichilemmoma in Cowden disease and sebaceous tumor in Muir-Torre syndrome[4]. Histologically benign tumors have a smooth border, uniform collection of epithelial cells, no necrosis, no atypia with none or minimal mitotic activity; while malignant tumors have cytonuclear pleomorphism, infiltrative borders, increased mitotic activity, necrosis with potential to metastasize. Surface ulceration is a common feature of malignant neoplasm[2].

Adnexal tumors are not very commonly encountered in pathology practice. For an accurate diagnosis, pathologist must be provided with data regarding age, gender, duration and rate of growth of tumor. These lesions are routinely diagnosed by their morphology on routine staining alone but on occasion special stains are needed. Advances in immunohistochemistry have shed new light on the relationship of different groups with each other as well as their histogenesis.[5]

METHODS

Twenty-four cases that were reported in Department of Pathology, Allama Iqbal Medical College, Lahore from 15thApril 2016 to 14th April 2017were

included in this cross-sectionalstudy. Relevant data regarding age, gender and history was obtained from the departmental record. Hematoxylin and eosin stained slides were examined in all cases. Periodic Acid Schiff with or without diastase was used where necessary.

RESULTS

Twenty-four cases of skin adnexal neoplasm were diagnosed in a period of one year. This number is quite low as compared to total number of surgical specimens received (0.31%). The male: female ratio was 1:2 (Table 1). Head and neck was the most commonly involved region (Table 2). The vast majority (83.3%) of tumors were benign (Table 3). Considering the histogenesis, tumors of sweat gland origin were the most frequent followed by those arising from hair follicle and sebaceous gland, respectively (Table 4, Fig 1). Proportion of malignant tumors was higher for those of sebaceous origin than for those of sweat gland and pilar origin (Fig 2, Fig 3). Photomicrographs (Fig 4-12) depict some of the important cases of the study.

Table 1: *Gender Distribution*

Serial no.	Gender	Number of cases	Percentage of cases
1	Female	16	66.66%
2	Male	8	33.33%
Total		24	100%

Table 2: *Frequency Distribution of Tumors According toLocation in the Body*

Serial no.	Site	No of cases	Percentage of cases
1	Head and neck	19	79.16%
2	Upper limb and trunk	3	12.5%
3	Lower limb	2	8.3%
Total		24	100%

Table 3: *Histological Categorization of Tumors*

Serial no	Nature of neoplasm	Number of cases	Percentage of cases
1	Benign	20	83.33%
2	Malignant	4	16.66%
Total		24	100%

Table 4: *Frequency Distribution According to Tissue of Origin of Neoplasm*

Serial no.	Tissue of origin	Number of cases	Percentage of cases
1	Sweat gland	12	50%
2	Pilar differentiation	9	37.5%
3	Sebaceous gland	3	12.5%
Total		24	100%

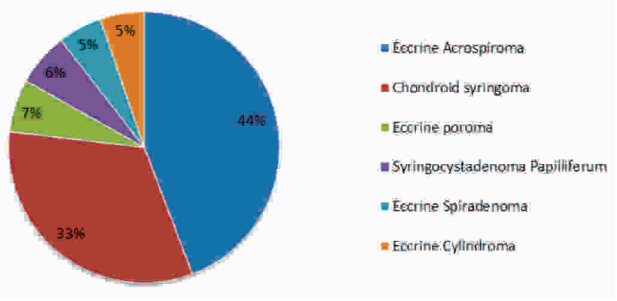

Fig.1: *Frequency Distribution of Tumors with Eccrine and Apocrine Differentiation*

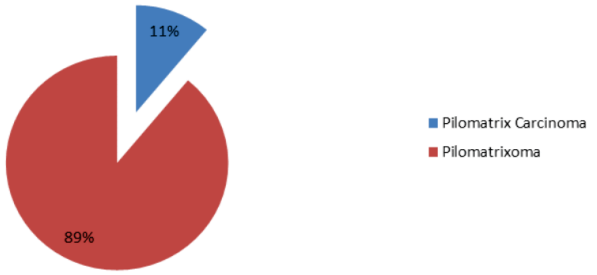

Fig.2: *Proportion of Malignancy in Tumors with Pilar Differentiation*

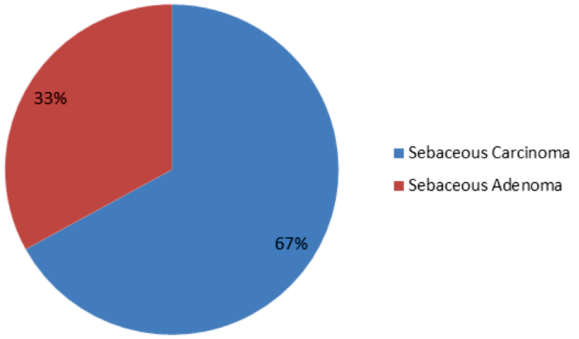

Fig.3: *Proportion of Malignancy in Tumors of Sebaceous Origin*

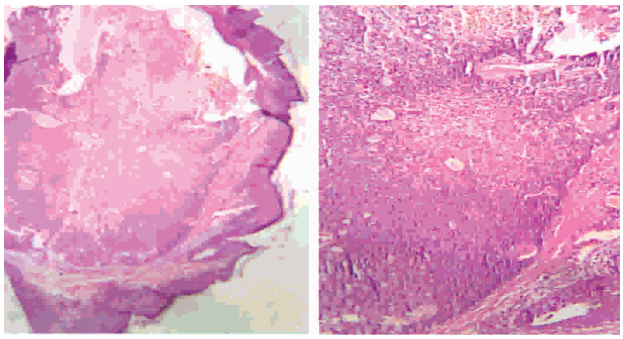

Figure 4. *Eccrine Acrospiroma A) Well Circumscribed Nodule in Upper Dermis (h & E, X40)b) Tumor Shows Dual Population Comprising of Clear Cells and Small Poroma Like Cells (H & E, X400)*

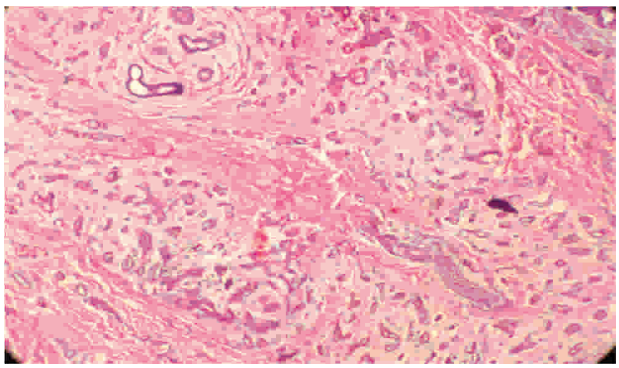

Figure 5. *Chondroidsyringoma: Cords and Ducts of Benign Epithelium in Myxoid Stroma (H & E, X100)*

Figure 6. *Eccrine Poroma: Sheets of Poroid Cells Showing Multiple Connections with Epidermis (H & E, X100)*

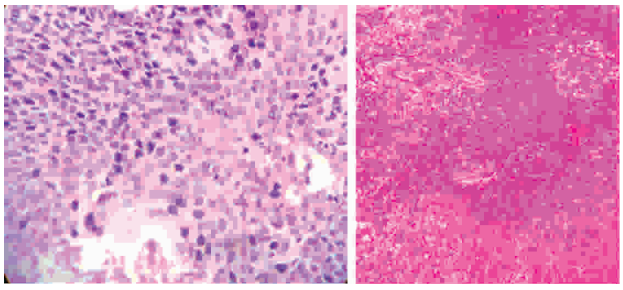

Figure7: *Porocarcinoma: A) Marked Pleomorphism in Poroid Cells (H & E, X100) b) PAS Staining in (X100)*

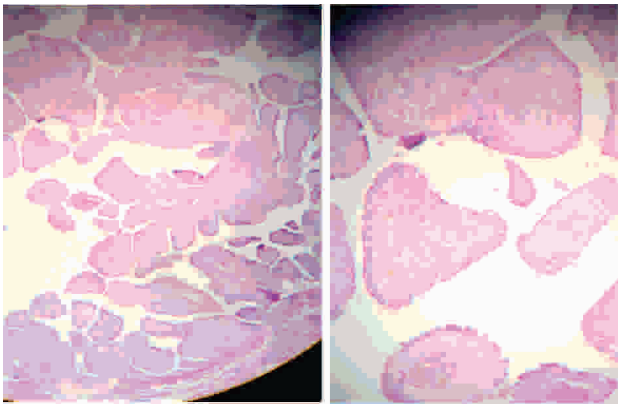

Figure 8. *Syringocystadenomapapilliferum: A) Papillary Projections Arising From Epithelium (h & E, X100) B) Dual Layer of Epithelium Lining The Papillae with Plasmacytic Infiltrate in Papillary Cores (H & E, X400)*

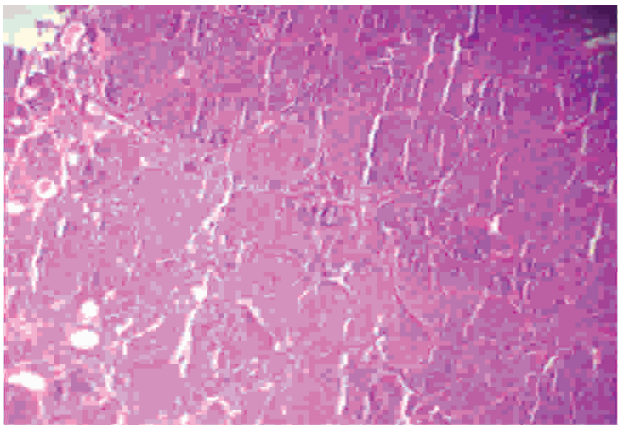

Figure 9: *Eccrine Cylindroma: Compact Nests of Basaloid Cells in Jigsaw Puzzle Pattern are Separated by Basement Membrane Material (H & E, X400)*

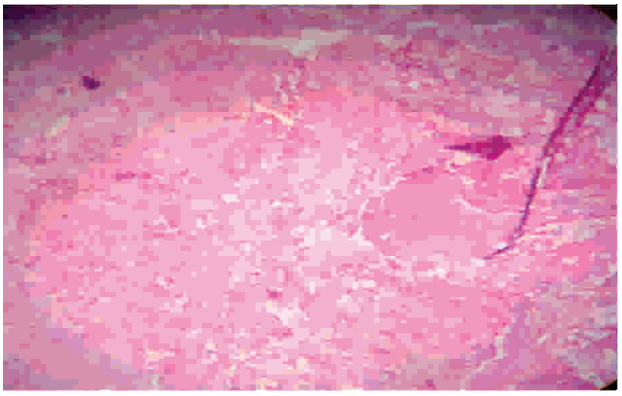

Figure 10: *Pilomatrixoma: Ghost cells in Piloma-*

trixoma (H & E, X400)

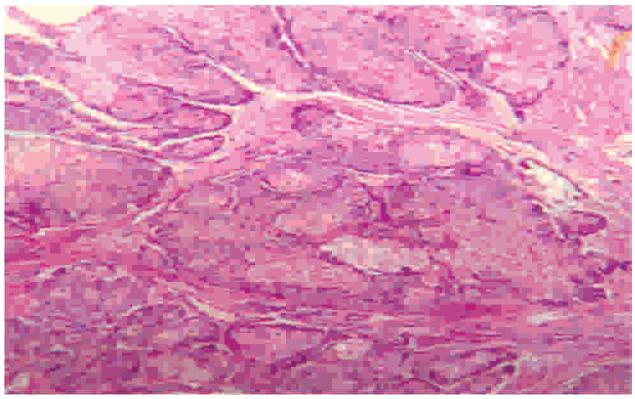

Figure 11: *Sebaceous Adenoma is Comprised of Variable Sized Lobules of Mature Sebaceous Cells (H & E, X100)*

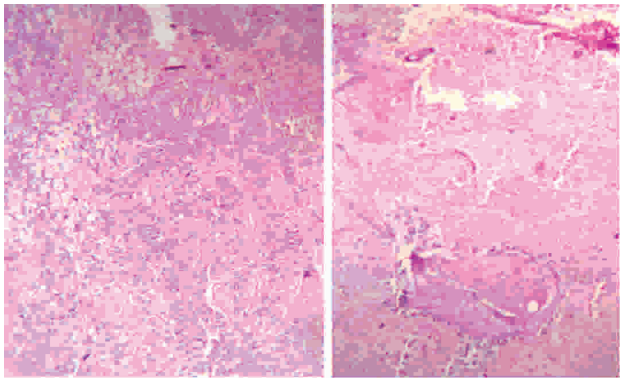

Figure 12: *Sebaceous Carcinoma: A) Tumor Cells Show Marked Cytological Pleomorphism with One Focus of Sebaceous Differentiation (h & E, X100) B) Extensive Necrosis in Tumor (H & E, X100)*

DISCUSSION

Skin adnexal tumors are a rare but challenging part of the histopathologist's practice.[6,7] They include a large variety of benign and malignant neoplasms with diverse histogenesis. The most widely held view is that they originate from different adnexal structures, but some contend that they arise from a common stem cell. [6]

In our study there was a remarkable female predominance. Similar results were observed in the study carried out by others[7,8] while slight male predominance is reported in the studies of Sharma et al and Yaqoob et al (M:F ratio 1.07:1).[9,10]

The most common region affected was found to be the head and neck (Table 2). This has been reported by other workers. [7,11]

Majority of the tumors (80%) were found to be benign (Table 3). This finding is supported by others.[7, 11,12] Benign tumors showed a wide age range of 9-50years while the malignant tumors appeared in older people with age range of 45-70 years.

Tumors of sweat gland were the commonest while tumors of pilar origin ranked second. Of these, pilomatrixoma (Fig 10) was the most common. These findings are supported by numerous other studies[7,9] except one by Kamyab- Hesariet al. that showed sebaceous gland origin being the commonest.[13] In our study three tumors of sebaceous origin were seen, of which two were sebaceous adenomas (Fig 11) and one was sebaceous carcinoma (Fig 12). Sebaceous neoplasms are mostly benign as has been reported elsewhere. [12]

One case of porocarcinoma was also encountered. This patient had an ulcerated lesion on her face. Face is the second most common location of poroid neoplasms.[9,14] Microscopically tumor showed infiltrative borders, cytonuclear pleomorphism, increased mitotic count and necrosis(Fig 7). Both clinical and microscopic features fulfilled the criteria of malignancy as ulceration itself is considered a sign of malignancy in these tumors.[2] In our patient it is possible that she had a poroma to start with that later underwent malignant transformation. This is supported by the long history of 3 years. Work on the evolution of porocarcinoma has suggested that it may be malignant from the beginning or arise in a long standing poroma.[15]

It is noteworthy that in our study, for both poroma and porocarcinoma, the most frequent site was found to be the head and neck region rather than hand and feet as reported by other workers.[16,17] Findings similar to ours have been published in other studies.[7,10]

CONCLUSION

It is concluded that frequency of skin adnexal tumor is quite low. Tumors of sweat gland origin are

the most common among the group. Head and neck region is the commonest site for skin adnexal tumors. Females are affected more than males. Benign tumors are typically seen in adults and middle age group while malignant tumors are prone to appear in middle to older age group. According to our study eccrine acrospiroma and pilomatrixoma are the most common tumors. Tumors with sebaceous differentiation have greater chances to be malignant than otheradnexal neoplasms.

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EFFICACY OF ENDOSCOPIC DILATION SESSIONS TIME SPAN IN TERMS OF RESOLUTION OF SYMPTOMS AND COMPLICATIONS

Jibran Umar Ayub, Samina Saeed, Khalid Mahmud Khan, Umar Ayub, Romana Inaam, Emaan Salam, Ayeslia Qaiser

Department of Medicine, Jinnah Hospital, Lahore

Abstract

Objective: The aim of this study is to compare the efficacy of weekly endoscopic dilation to fortnight sessions in context of resolution of symptoms and complications.

Materials and methods: A randomized controlled trial was conducted at East Medical Ward Mayo Hospital Lahore. A total of 50 patients were included in this study. For the first endoscopic session, patients were kept nil by mouth and dilation was conducted under fluoroscopic guidance. Patients were randomized (using computer generated random process) into two groups, group A for weekly follow up sessions and group B for fortnightly sessions. Statistical analysis of the data was performed using SPSS version 20.

RESULTS: Mean age of patients was 27.20±8.67 years with minimum and maximum age 15 and 43 years respectively. Gender distribution of patients showed that there were 42% male and 58% female patients, Dysphagia for solids and liquid was significantly reduced in case of weekly dilation treatment, However, no significant differences in context of complications as cough, vomiting and retrosternal pain were observed for both cases, one week and two weeks treatments during course of follow up time period. Vomiting at 1st week and weight gain at 4th and 8th week were the significant differences in two different treatment group. However, weight gain was high for group B, who received fortnight treatment. However 6 patients in Group-A and 8 patients in Group-B were lost to follow up. Among these lost to follow up patients, one patient had perforation and referred to chest surgery department and lost to follow up. However 1 patient had tracheoesophageal fistula which was also lost to follow up and referred to chest surgery. Remaining 12 patients lost to follow up reason were not known.

CONCLUSION: Based on the results, it is suggested that weekly endoscopic balloon dilation treatment is more effective due to significant decrease in dysphagia condition as compared to fortnight folio AY up treatment and no obvious differences were observed in after treatment effects such as coughing, vomiting and retrosternal pain etc.

KEY WORDS: endoscopic dilation. resolution of symptoms, complications

Esophageal stricture is defined as nan owing of the esophagus that causes difficulty in swallowing of solids and liquids. Esophageal strictures can be caused by malignant or benign lesions. Patients experience dysphagia for solids and liquids with primary symptoms, regurgitation, respiratory complaints (nocturnal cough, aspiration), retrosternal pain and weight loss regardless whether their strictures are caused by malignant or benign lesions. A large number of diseases can lead to formation of esophageal stricture that includes acid peptic, autoimmune, post infectious, secondary- to caustic agents, congenital and iatrogenic. Approximately 70-80% of esophageal strictures arc due to Gastroesophageal reflux diseases.[1,2] Postoperative strictures are repor-ted about 10% and corrosive strictures account for a small percentage about 5%.[3,4] Intake of corrosives is a key factor of benign strictures.[5-7] These corrosive include household cleaning agents, chemicals like lye. acids, alkalis etc. and sometimes injuries are deemed to be more catastrophic, if it is intentional with large volume ingestion which lead to serious

Correspondence: Jibran Umar Ayub Khan, Harrogate District Hospital UK. Email: jibranumar@yahoo.com

consequences in form of lifelong debilitating conditions and esophageal carcinoma. The mortality rate after corrosive ingestion is significant that is reported to be as alarming as 20%.[5,8]

Different approaches such as, balloon dilatation, botulinum toxin injection, and surgical intervention (Heller myotomy) are employed to relieve symptoms. However, the effectiveness of balloon dilatation and botulinum toxin injection require repeated treatment. Surgical option is seldomly required and only performed in case a stricture cannot be dilated enough to permit solid food to go through or if repeated sessions are unable to prevent recurrence of strictures.[3,7] Pneumatic dilatation is an effective, safe, noninvasive and relatively cost-effective approach. The minimal pain, suitable to any age group and even during pregnancy are advantages of pneumatic dilation over other approaches. However the esophageal manometry is important to follow-up. The appropriate time span to repeal treatment or modify treatment modalities is still uncertain and require further investigations and understanding The two methods of dilation are performed either by passing a dilator (Savary) or air-filled balloon (TTS balloon) through an endoscope. However, the best method for dilatation and type of stricture amenable to treatment is still a question mark. Repeated sessions are usually required to prevent the stricture recurrence. Relatively the morbidity and mortality that is associated with esophageal dilatation is low as compared to surgery.[8] In common practice the interval between dilation sessions depends on individual circumstances in which the possibility of early resolution is weighed against possibility of complications. But optimal timing of follow up sessions of dilatation is still a matter of debate and needs to be evaluated with properly designed studies. The present study is designed to compare the efficacy of weekly and fortnight endoscopic dilation sessions in terms of resolution of symptoms as well as complications.

METHODS

Study Design; It was a randomized controlled trail conducted at East Medical Ward Mayo Hospital Lahore

DURATION OF STUDY: Data was collected in six months.

SAMPLE SIZE: This study was conducted on 50 patients with esophageal strictures caused by corrosive ingestion.

SAMPLING TECHNIQUE: Non probability purposive sampling.

SAMPLE SELECTION

The subjects (patients) included in this study have age in range of 15-50 years male and female (M/F). Patients have the history of corrosive ingestion, dysphagia for solids, esophageal stricture secondary to corrosive ingestion and failure to pass upper GI endoscope across stricture. Patients were diagnosed with malignant strictures based on histopathology of endoscopic biopsy. Patients having esophageal strictures due to peptic ulcer diseases, congenital esophageal strictures, stricture due to repeated EVBL, not fit for endoscopy, refusal to participate in the study, Achlasia Cardia. and female patients with Pregnancy were excluded in this study.

DATA COLLECTION PROCEDURE;

Approval of the ethical committee was sought and all ethical considerations were fulfilled. The consents from all patients included in this study were obtained after explaining them about all the pros and cons and patients' identification was kept highly confidential. Thorough history of each patient was taken and a detailed physical examination was performed for each patient. The stricture position, length and degree of narrowing of esophageal lumen was determined through barium swallow and barium meal for each individual patient. Patients were randomized into group A for weekly follow up sessions and group B for fortnightly follow up sessions. For the first endoscopic dilation session, die patient was kept nil by mouth and dilation was conducted under fluoroscopic guidance. Dilation was done with TTS balloon or Savary (10mm/

Savary 27F) at the start. The repeated dilation sessions were carried out in an incremental fashion (30-36-45F) i.e, in follow up session the size of dilator was increased by 2mm in each successive session till 15mm. Dilatation was considered adequate wing the esophageal lumen could be dilated up to 15mm.Whenever there was a suspicion of complication such as perforation during dilatation, an urgent chest X-ray and oesophagogram using a water soluble contrast medium w as performed. The patient was performed the possibility of perforation was ruled out. In case of confirmation of perforation, the patient was given intravenous fluids and antibiotics and was advised to take nothing by mouth. An immediate surgical consultation was sought and the patient w as managed jointly with the surgical team, The outcome of treatment was judged on the basis of improvement in dysphagia, which was graded as follows:

Grade 0: taking a normal diet, Grade 1: unable to swallow certain solids, Grade 2: can swallow only semisolid soft diet; Grade 3; can swallow liquids only, Grade 4: unable to swallow even liquids in adequate amounts.

After an adequate initial dilatation (15mm), patients were instructed for follow up weekly and fortnightly intervals Repeat dilatation up to 15 mm was done in case of dysphagia recur. During recurrence, dilatation was done without any radiological evaluation of the esophagus. If dysphagia persisted despite dilatation, barium swallow examination was performed to assess the esophageal lumen, ff the symptoms persisted after three months period of endoscopic dilatation, the patient was referred for surgical treatment.

DATA ANALYSIS

Statistical analysis of the data was performed using SPSS version 16. Mean±SD deviation was calculated for continuous variable like age. Male to female ratio was calculated for gender. Success rate of corrosive esophageal strictures dilatation by endoscopy between two groups was compared in terms of number of sessions needed: trine taken for

Table 1: *Statistical Analysis Symptoms (Dysphagia for Solids. Dysphagia for Liquids, Cough, Vomiting, Retrosternal Pain and Weight Gain) Reported by the Patients, Received Esophageal Strictures Dilatation.*

No. of Weeks	Group		P-Value	Loss to Follow Up
	A	B		
Dysphagia for Solids				
1st	8(32%)	16(64%)	0.023	0
4th	7(28%)	4(16%)	0.307	0
8th	1(4,76%)	0(0%)	0,555	10
16th	1(4,76%)	0(0%)	0.580	11
24th	0(0%)	0(0%)	0.957	14
Dysphagia for Liquids				
1st	6(24%)	12(48%)	0,077	0
4th	4(16%)	4(16%)	-	0
8th	3(13.63%)	0(0%)	0.166	10
16th	1(4.76%)	0(0%)	0.580	]]
24th	0(0%)	0(0%)	0.957	14
Cough				
1st	2(8%)	6(24%)	0.122	0
4th	4(16%)	6(24%)	0.479	0
8th	2(9,09%)	4(22,22%)	0,248	10
16th	2(9,09%)	2(11,76%)	0.784	11
24th	0(0%)	0(0%)	0,957	14
Vomiting				
1st	3(12%)	12(48%)	0.005	0
4th	8(32%)	6(24%)	0.528	0
8th	9(40.90%)	8(44,44%)	0.822	10
16th	2(9.09%)	2(11.76%)	0.784	11
24th	0(0%)	0(0%)	0.957	14
Retrosternal Pain				
1st	6(24%)	12(48%)	0.077	0
4th	15(60%)	17(68%)	0,555	0
8th	6(27,27%)	15(83,33%)	0,000	10
16th	4(18,18%)	7(41,17%)	0,113	11
24th	0(0%)	0(0%)	-	14
Weight Gain				
1st	3(12%)	8(32%)	0.087	0
4th	4(16%)	11(44%)	0.030	0
8th	4(16%)	9(36%)	0.032	10
16th	4(16%)	7(28%)	0.113	11
24th	3(12%)	3(12%)	0.881	14

Group-A= Weekly follow up. Number of Patients =25
Group-B= Fortnight follow up. Number of Patients =25

symptoms relief and complications developed using chi-square test and independent / Mann Whitney U-test two tailed t test. Data was expressed in the form of cross tabulation (Table 1) and graphs (Figure 1).

RESULTS

Mean age of patients included in this study was 27.20±8.67 years with statistically insignificant difference in both Group A and B with gender distribution 42% male and 58% female patients. At 1st week, 8(32%) patients in Group-A and 16(64%) patients in Group-B had dysphagia for solids, statistically higher in group B as compared to group-A with p-value < 0.05 (Figure 1(a)). At 4th week, 7(28%) patients in Group-A and 4(16%) patients in Group-B had dysphagia for solids with equal statistical significance with p-value > 0.05. From 8th to 24th weeks, no significant difference was seen in patients for dysphagia for solids in both groups with p-value > 0.05. After 16th week, 6(24%) patients in Group A while 8(32%) patients in Group B were lost to follow up. The loss to follow up of patients may be due to their recovery.

At 1st week. 6(24%) patients in Group-A and 12(48%) patients in Group-B had dysphagia for liquids, p-value < 0.05 (Figure 1(b)). At 4th week 4(16%) patients in each group had dysphagia for liquids. From 4th to 24th weeks, no statistically significant difference was seen in both treatment groups for dysphagia for liquids, p-value > 0,05. The 2(8%) patients in group A and 6(24%) patients in group B reported cough at first follow up. w ith insignificant difference, p-value > 0,05 (Figure 1(c)). The statistical insignificant difference was seen at each follow up sessions weekly as well as fortnight, p-value regarding cough. In Group-A. 3 (12%) patients at 1st week. 8 patients at 4th week, 9 patients at 16th week. 2 patients at 24th week and none of the patients at last follow7 up had vomiting (Figure 1(d)), In Group-B, 12 patients at 1st week. 6 at 4th week. 8 at 8th week and 2 patients at 16th week had reported vomiting symptoms. Although no statistically significant difference was observed in both treatment groups except at 1st week.

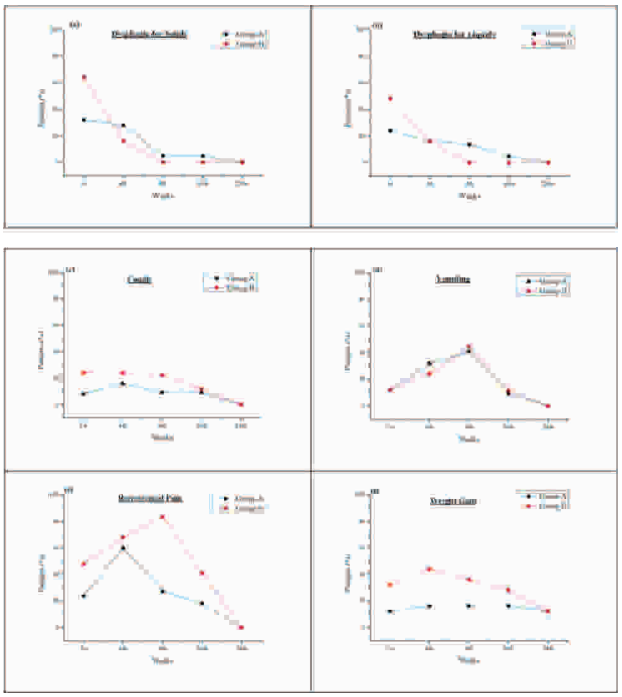

Figure 1: *Statistical analysis of symptoms as (a)Dysphagia for Solids, (b) Dysphagia for Liquids, (c)Cough, (d) Vomiting, (e) Retrosternal Pain and (f)Weight Gain, reported by the patients received esophageal strictures dilatation by endoscopy for lime period of six months.*

The observed trends showed that the occurence of vomiting was lower in Group-A patients. Moreover during follow up time period, it was observed that retrosternal pain was high in Group-B patients as compared to Group-A patients (Figure (e)). However at 8th week significant difference for retrosternal pain was observed in both groups. Patients who wore treated on weekly basis, experience less retrosternal pain. Lastly, the weight gain was high at 4th and 8th week with p-value < 0.05 in Group-B (Figure 1 (f))- Among lost to follow up patients, one patient had perforation which was referred to chest surge ry department and was lost to follow up. However 1 patient had tracheoesophageal fistula which was also lost to follow up and referred to chest surgery. Remaining 12 patients lost to follow up reason were not known.

DISCUSSION

The ingestion of caustic agents can result in extensive damage to the gastrointestinal tract that can lead to different complications with subsequent morbidity, which requires prolonged stay in hospital. In the acute selling, the severe damage can cause esophageal perforation and worst sequel in form of death. The long term complications such as esophageal sincere (ES) and gastric outlet obstruction (GOO), may develop after a time period from few weeks to years after intake of caustic agents.[9,10] ES and GOO are two entirely separate entities and they often occur independently, but for patients affected by the ingestion of corrosive agents, they are reported simultaneously present in different cases up to 20%.

Endoscopy is utilized to ascertain the degree as well as die extent of damage of gastrointestinal tract within the first 48 hours, and later on can be used as a modality of treatment of strictures developed in both esophagus and stomach.[11-13] Different researches suggested that die use of endoscopic balloon dilation (EBD) to treat eorrosives-induced ES or GOO in isolation has proven an effective way in majority cases. On the contrary the EBD as a method to treat patients who have ES and GOO at the same time is not formally evaluated. In case of simultaneous presence of ES and GOO. the endoscopic treatment may turn more complicated. Endoscopy should be avoided within 2 weeks after corrosive insult apparent due to escalating risk of perforation in this time period.[14,15] But there are no concrete evidences in the literature to suggest the optimum timing to execute endoscopic balloon dilation sessions, EBD can be performed about four to six weeks elapse since corrosive injury and is considered the treatment of choice for majority of such injuries.[13,16,17]

For patients with ES, esophagectomy followed by reconstruction operation is also an option but it is highly invasive procedure for both the patient and the surgeon, It is performed only in severe circumstances, when EBD fails or the patients is unable to tolerate EBD. Unlike ES, surgical treatment for GOO is subtotal gastrectomy or bypass gastrojejunostomy, which is not dangerous and can be done with fewer complications ranging from 0% to 10.7%. Therefore, surgery can be effectively used as a modality of choice for GOO. Recently. Kochhar and companions suggested that EBD is a safe cum effective treatment for patients with corrosive induced GOO and the relief of symptoms could be successfully achieved in 95.1% cases with a minor perforation rate (2.4%).[18,19] Paulo Fernando Souto Bittencourt suggested that th^ endoscopic dilatation of esophageal strictures yields better results in most cases with lesser complications. Patients with esophageal stricture as consequence of caustic ingestion have higher morbidity and requires repeated dilatation sessions. Patients must be treated on individually, even when the underlying etiology is identical.

In present study, a comparison was carried out on the effectiveness of weekly endoscopic dilation as compared to 2 week sessions in terms of resolution of symptoms as well as complications. The Group-A (patients who received weekly dilation) till last follow up 24th week, 6 patients were lost to follow up, While in Group-B till 24th week, 8 patients were lost to follow up Results inferred that dysphagia for solids and liquid showed no significant difference for both groups A and B during follow up time period. A slight high dysphagia for solids liquid in Group-B is observed in 1st week as compared to Group-A, For the rest of weeks, no significant difference was observed. Vomiting at 1st week and weight gain at 4th and 8th week showed statistically significant difference in both treatment groups. However at 4th and 8th week, the weight gain was high in Group-B patients as compared to Group-A patients.

Yi-Chun Chiu reported the effects of endoscopic-guided balloon dilations (EBB) in patients with upper gastrointestinal strictures due to corrosive ingestion in both ES and GOO separately as well as in case of concurrent occurrence of ES + GOO. It was observed that the success rate for both groups vary, better in ES group as compared to ES + GOO group (83.3% vs. 57.1% vs. 36.4% p = 0.035). Fewer complications were observed in ES group than ES + GOO group (16.7% vs. 42.9% vs, 36.4%,

p- 0.041). GOO +ES group needed more sessions of dilations in order to achieve success dilations as compared to ES group. (13,7 ± 4.9 vs. 6.1 ± 4.7 vs. 5.5±2.1, p=0.011).[20] Paulo Fernando Souio Bittencourt assessed the main causes of esophageal stricture in pediatric age group and their ultimate response to endoscopic dilatation Esophageal perforation was reported in five cases and one case of hemorrhage due complication of the procedure. Adequate response to endoscopic treatment was found in 74.4% cases, but better results were seen in patients with peptic esophageal stricture.[1] Sajida Qureshi evaluated the endoscopic dilatation of benign esophageal strictures and its outcome. In has reported that mean dilatation frequency for strictures longer than 5cms was 7.10±5.322 vs. 3.47±3.281 for strictures <6cms (p<0.037). Corrosive strictures were seen more common in the upper esophagus as compared to peptic (Mean 22.44 ± 5.240 cm vs, 30.20 ± 4.780 cm), p0.001. Only 81.4% corrosive stricture could be adequately dilated at initial dilatation as compared to 100% in peptic strictures. Mean symptomatic recurrences per month were 0.6919 ± 0.300 in corrosives and 0.365 ± 0.293 in peptic strictures (p<0.003). There were 4 procedure related perforations among all patients with corrosive strictures. Overall mortality 7.4% was reported.[22] Sher Rehman determined the outcome of esophageal dilatation in caustic esophageal strictures in patients. Successful dilatation up to a lumen size of 15mm was achieved in twelve patients (60%). Six patients (30%) were referred for surgery due to complications and two patients (10%) had perforation with an incidence rate of 0.45%.[23]

Interval between repeated dilation sessions may depend on individual circumstances in which the possibility of early resolution is weighed against possibility of complications But optimal timing for follow up dilation sessions is still a matter of debate and needs appropriately designed investigation. Although different time interval are used for dilation procedure i.e. 1-3 weeks, however the literature suggests the weekly dilation in sub-acute phase of caustic ingestion to facilitate: (a) reaching the end point of 15 mm in a short period of time; and (b) maintaining nutritional status of the patient. For patients with chronic phase of caustic ingestion and pcptic-GOO. dilation can be performed once a week or once in 3 weeks. Once the adequate nutrition is ensured, the interval between dilations can be varied, taking into account the social circumstances; e g. the distance patient travels.

CONCLUSION

Based on the results of present study, dysphagia for solid and liquid did not show any statistically signification association in relation to treatment groups. However, the dysphagia for liquid was high 0-68% in Group A as compared to Group-B patients i.e. 0-48%, The presence of cough and vomiting in Group-A patients was low as compared to Group-B patients. Similarly retrosternal pain was observed to be high in Group-B patients. While weight gain status in Group-B patients was better, ranges between 0-52% as compared to Group-A patients i.e. 8-16%. Keeping these results in mind it is suggested that weekly endoscopic balloon dilation is more effective than fortnight follow up sessions.

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INFECTION OF ACINETOBACTER BAUMANNII AND IT'S RESISTANT PATTERN IN A TERTIARY CARE HOSPITAL OF LAHORE; PAKISTAN

Hina Bukhari[1], Amna Sabir[2], Tayyab Hassan[3], Muhammad Ejaz[4], Muhammad Abdul Rehman[5], Imtenan Shahid[6]

Abstract

Objective: To Find increasing occurrence of Acinetobacter baumanii as a result of spread of noso-comial infection and to take effective steps to decrease it's spread by regular surveillance and fumigation of wards , operation theaters and ICUs.

Methodology: This is a cross-sectional study carried out from April 2018 to September 2018. Specimen were assembled and handled through the normal route of laboratory work. The clinical samples were collected from the patients admitted in indoor (wards & ICUs) of the hospital. A total number of 6360 samples were received. All samples were processed according to standard guidelines. For further confirmation of Acinetobacter baumannii a series of biochemical test were also performed. Antibiotics susceptibility analysis done according to the guidelines of Clinical laboratory Standards Institutes 2018.

Results: Out of 6360, 297 were positive for Acinetobacter baumannii. Prevalence of Acinetobacter baumannii was 4.67 %. All strains were sensitive to Colistin, Polymyxin b and Tigecycline.

Conclusions: With Each passing day pan-resistant Acinetobacter baumannii are emerging so we should formulate empirical schemes for the use of antibiotics in the hospitals in view of the emerging resistance.

In addition measures should be taken to prevent spread of Acinetobacter species by means of hospital workers and surveillance should be done every so often to prevent in hospital spread.

Key Words: Acinetobacter baumannii, Resistant Pattern of Acinetobacter baumannii, multi-drug resistant

With each passing day Acinetobacter baumannii is emerging as a notorious and difficult to treat nosocomial pathogen.[1,2] Martinus willem Beigerinck first discovered Acinetobacter in the year 1911. In year 1970 this started establishing its position as a notorious hospital associated micro-organisms. These are immotile, catalase positive but indole, urease & oxidase negative bacteria. Acinetobacter baumannii forms biofilms rendering it resistant to disinfection.[3,4] Acinetobacter belongs to gram negative bacteria which are non-fermenters. It is coccobacilli in shape. It is universal in its presence but it is most wide spread in stifling tropical regions of world. It is present in warm and humid areas of humans but this stay is temporary so mostly does not result infection.[1] It has the proficiency of triggering respiratory tract infections particularly in patients on ventilators, urinary tract infections, wound infections, infection of meninges, endocarditis and septicemia.[1,2] It has been able to survive under hostile environmental circumstances[2]. It is widely distributed in soil, food, water and sewage.[4]

Bacteria attach, colonize and thrive resulting in infection and damage to body tissues. Wounds offer ideal setting for micro-organisms to thrive. Internal tissues of body are usually free from any pathogens in disease free health individuals; nevertheless, the skin surface is populated by a lot of micro-organisms largely bacteria. These bacteria are part of normal flora but when the barrier of skin is disrupted these micro-organisms populate wounds and can enter into blood-stream. Wound infections belong to one

Correspondence: Dr Amna Sabir, aaminahdoc@gmail.com

of the most common type of infections and resulting morbidity and mortality is very high. Mortality can be up-to 70-80 percent.[5]

Classically carbapenems are used for cure of infection caused by Acinetobacter baumannii. Resistance to carbapenems is emerging day by day and it is becoming a problem for the whole.[6] Carbapenems mostly used as first line therapy for Acinetobacter species include meropenem and imipenem.[7] Multi-drug resistant Acinetobacter species has arisen as a gigantic problem over past years. For multi-drug resistant Acinetobacter species drugs of choice are Colistin, tigecycline and polymyxin B.[1,8-11]

Pan-resistant Acinetobacter baumannii is also reported with emerging strains resistant to Colistin in some parts of earth.[10-11]

METHODS

Objectives:

To Find increasing occurrence of Acinetobacter baumannii as a result of spread of noso-comial infection and to take effective steps to decrease it's spread by regular surveillance and fumigation of wards , operation theaters and ICUs.

Methodology

It is a cross-sectional study carried over a period of 6 months from April 2018 to September 2018.

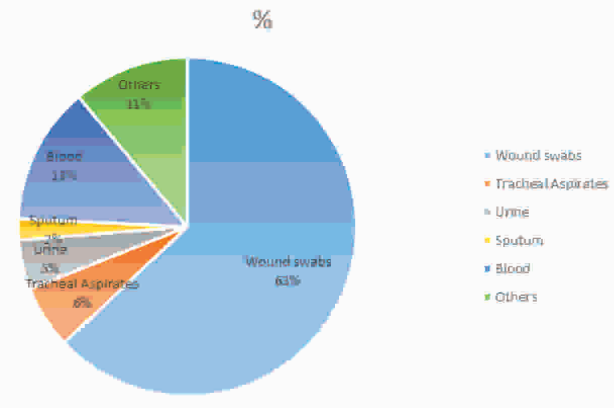
This study was carried out in Microbiology section Pathology laboratory of King Edward Medical University attached to Mayo Hospital Lahore. Specimen were assembled and handled through the normal route of laboratory work of the clinical samples from patients in In-patient Departments (wards & ICUs) of the hospital. A total of samples 6360 were received. All samples were processed according to standard guidelines. For further confirmation of Acinetobacter baumannii a series of biochemical test and API NE(Biomerieux) was also used.

Antibiotics susceptibility analysis done according to the guidelines of Clinical laboratory Standards Institutes 2018.

Results:

This study was conducted from April 2018 to September 2018. A total of 6360 samples were received from different age groups and different departments of hospital. For calculation of results Spss version 26 is used.

Isolation of Acinetobacter baumannii from different clinical samples was shown in Pie Chart-1. Out of these 297 were positive for Acinetobacter baumannii. Prevalence of Acinetobacter baumannii was 4.67 %. All strains were sensitive to Colistin, Polymyxin b and tigecycline. Maximum resistance was shown by Trimethoprim – sulphamethoxazole. 97.64%. Most of strains were sensitive to piperacillin- tazobactam with 25% strains showing resistance. Meropenem and Imipenem were resistance in 94 isolates of Acinetobacter baumannii. Results are shown in Table-1. Table-3 shows percentage of Acinetobacter baumannii isolated from various In patient and out patient department.



Pie Chart 1- *Isolation of Acinetobacter Species from Various Clinical Samples*

DISCUSSION

Acinetobacter sp. is emerging as most commonly encountered source of noso-comial infection second in number to Pseudomonas species[2,3]. It is also becoming source of outbreaks in hospitals[2]. Acinetobacter have emerged as a substantial class of pathogenic bacteria, constantly creating hazards to our national healthcare routine.[13]

Factors associated with spread of Acinetobacter

Table 2: *Antibiotics resistant pattern of Acinetobacter baumannnii isolates (n=297)*

Antibiotics group	No. Of resistant Isolates (n=297)	% Of resistance
Amikacin	178	60%
Cefotaxime	268	90.2%
Ceftriaxone	268	90.2%
Cefepime	212	71.4%
Ciprofloxacin	262	88%
Gentamicin	178	60%
Imipenem	94	31.6%
Meropenem	94	31.6%
Sulfamethoxazole-trimethoprim	290	97.64%
Polymyxin B	0	0%
Tigecycline	0	0%
Colistin	0	0%

Table 3: Sources of Acinetobacter Isolates (n=297)

Sources	No. Of resistant Isolates (n=297)	Percentage %
ICUs	173	58.25%
Surgical Departments	76	25.59%
Medicinal Departments	37	12.46%
Outpatient Departments	11	3.71%

baumannii include assisted ventilation, catheterization, and surgery. In addition earlier use of antibiotics and long ICU stays have also been found to be responsible for its outbreaks in hospitals.[14,15]

In This study prevalence of Acinetobacter baumannii was 4.67% which was similar to studies by suryawanshi NM et al (5.2%)[2] and Vaja et al (4.8%)[4]. In other studies higher prevalence was seen 9.1 % in Dam S et al1 and 14% by Mostofi et al[12].

In this study all isolates were sensitive to Polymyxin B, Tigecycline and Colistin similar to results seen by Dam S et al1 and Surayawansh Nm et al[2]. Because these were selectively used for carbapenam-resistant gram-negative bacteria.

Carbapenams were used as a drug of choice for Acinetobacter baumannii but now these organisms are becoming resistant to these drugs which each passing day. This study concluded that we should take measures before using antibiotics. We should limit the use of antibiotics to conditions where they are justified. Usage should be for the recommended duration in recommended dosage.[3]

We should formulate empirical schemes for the use of antibiotics in hospitals in view of the emerging resistance.[2]

In addition measures should be taken to prevent spread of Acinetobacter species by means of hospital workers and surveillance should be done every so often to prevent in hospital spread.[4]

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SAFETY, EFFICACY AND ACCEPTABILITY OF SUB DERMAL CONTRACEPTIVE IMPLANT EXPERIENCE AT JINNAH HOSPITAL LAHORE

Zareen Amjad, Amtullah Zarreen, Sara Saeed, Naila, Gulshan

Department of Gynaecology/Surgery, Jinnah Hospital/Allama Iqbal Medical, Lahore

Abstract

Abstract: Progestin-only contraceptive implants are a highly effective reversible contraceptives Acceptability and continuation by clients is growing high. Menstrual irregularities are most common symptoms that can be well managed by pre insertion counseling. Headache, weight gain , acne and breast tenderness are other adverse effects.

Objective; To study Safety, efficacy and acceptability of Progesterone containing sub dermal contraceptive implants among women at Jinnah Hospital Lahore.

Material and method; A study conducted at Gynae unit 1 in collaboration with Family planning centre at Jinnah Hospital Lahore from June 2015-June 2018. Implanon was available from June 2015- Dec 2016 and 312 insertions were done. Jadelle was available from Jan 2017 onwards. 300 women had jadelle insertion from Jan 2017-June 2018. Follow up with implanon was completed and women with Jadelle insertion are still in follow ups.

Results: 612 women participated in study. 312 had implanon while 300 had jadelle insertion.67% 0f women were using contraception previously. None of them had previous exposure to contraceptive implant. Irregular vaginal bleeding was commonest side effect faced by 27% of women with implanon. 40% of women having Jadelle had prolonged heavy vaginal bleeding. Menstrual irregularities were present in 100% of women with Jadelle while 67% with Implanon. There was no difference in both implants regarding other adverse effects like headache, weight gain, breast tenderness and acne. Acceptability and satisfaction was found to be high with implanon.

Due to their high efficacy and safety contraceptive implants have been licensed in over 60 countries in the world and used by millions of women for over four decades. Other then above mentioned benefits of the implants, they are user friendly ,have long duration of action, non proble-matic during intercourse, client is unaware of implant presence, and fertility returns immediately after removal.[1] Norplant was first sub dermal contraceptive implant containing levonorgestril, introduced in market in 1983 and withdrawn globally in 2008 due to its difficult insertion, removal and complications. Researchers centered on to facilitate insertion and removal easy and reducing side effect profiles. Another Levonorgestril containing implant Jadelle was launched in the United States in 1996. Shortly after this in 1999 Implanon, a new implant containing Etonogestril was introduced. In 2010 Implanon NXT was introduced and now being widely used in many countries worldwide.[2] JADELLE is a set of two flexible cylindrical implants, each containing 75 mg of the progestin levonorgestrel. The total administered (implanted) dose is 150 mg. Dail release rate of levonorgestrel provided by the implants is about 100 µg/day at END OF Ist Month, followed by a decline to about 40 µg/day at 12 months and to about 30 µg/day at 24 months and beyond.[3] Implanon is single rod containing 68 mg of etonogestrel (progestogen). Plasma levels of ENG(etonogestrel) sufficient to inhibit ovulation (>90 pg/mL) are achieved within 8 hours of insertion. Ovulation returns within 3 weeks of implant removal in more than 90% of women.[4] These sub dermal contraceptive implants act by inhibiting ovulation and increasing viscosity of cervical mucus.[5] Irregular periods, weight gain, acne, headache and breast tenderness are commonly experienced side effects.[6]

METHOD

A study was conducted in Jinnah hospital Lahore in Gynae unit 1 From June 2015- June 2018 to assess safety, efficacy and acceptance of sub

dermal contraceptive implants by users at Jinnah hospital Lahore. Study conducted in 2 parts depending upon the availability of subdermal implants. Implanon available from Jan 2015- December 2016. 312 insertions done. From 2017 only Jadelle available and 300 insertions done from Jan-2017-june 2018. Total number of clients was 612 in 36 months.

Informed consent was taken. Adequate information about Implants was revealed to the women regarding type of contraception, mechanism of action and insertion and removal .Pre designed proforma filled regarding patient's information in terms of age, parity, mode of delivery, previous contraception. In addition to this bleeding complications, other adverse effects ,satisfaction rate of patients and reasons for removal of implant also noted.

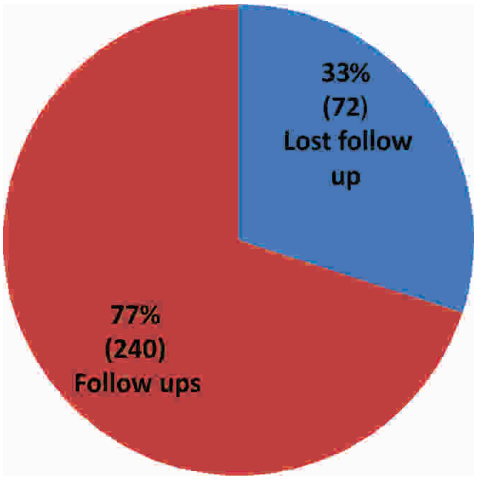


Figure 1: *Follow up with implanon*

Table 1: *Patients Demographics*

Age(years)	N=612	%
Less than 20	101	16.4
20-30 years	370	60.5
More than 40	141	23

Table 2: *Parity of Patients*

Parity	N=612	%
P1-2	176	28.8
P3-4	357	58.3
P5 or more	79	12.8

Table 3: *Mode of Delivery*

Mode of delivery	N=612	%
Cesarean section	367	60
Vaginal delivery	245	40

Table 5: *Menstrual Irregularities with Implanon*

Complications	N=240	%
Irregular vaginal bleeding	65	27
Amenorrhea	36	15
Prolonged heavy bleeding	48	20
Prolonged spotting	43	18
Normal menstruation	28	20

Women Acceptability of Jedelle

Comparison of Implanon and Jedelle regarding side effects profile

Other adverse effects

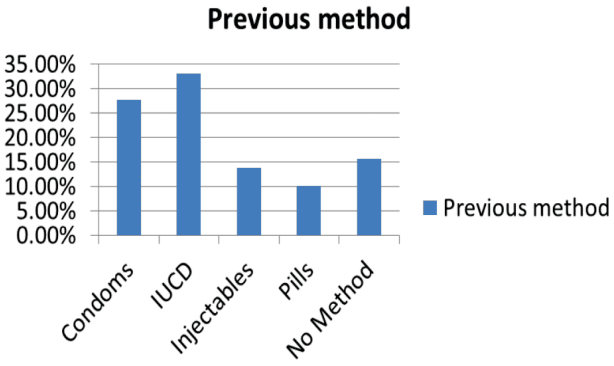


Figure 4:

DISCUSSION

Millions of implants having been inserted

Table 6: *Adverse effects of Implanon other than Menstruation*

Adverse effects	N=240	%
Headache	81	34
Weight gain	48	20
Mood swings	19	8
Mastalgia	22	9
No Symptoms	70	29

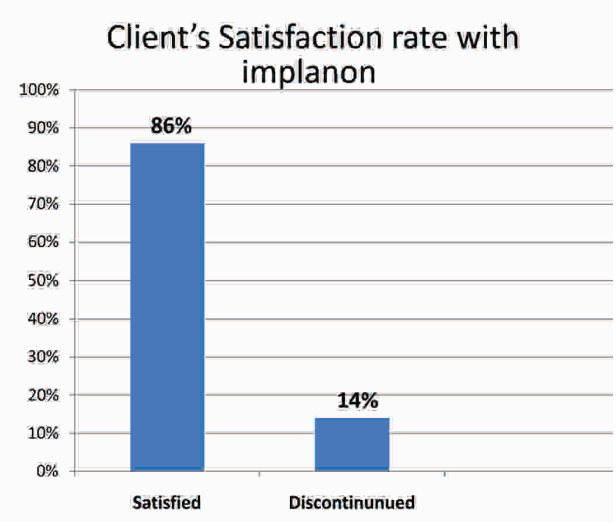


Table 7: *Removal of Implanon*

Total insertions	Removal	
312	84	72 completed tenure 12 removed due to complications

Table 8: *Insertion of Jadelle (Available since 2017 in Jinnah hospital lahore)*

Total insertions	360
Follow ups	260
Removal	Nil

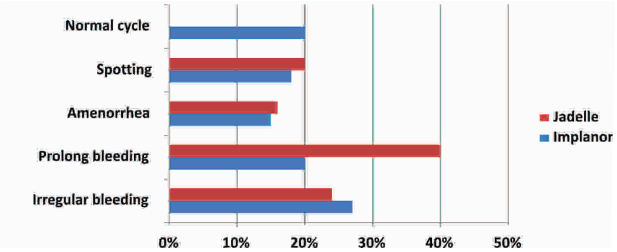
Table 9: *Menstrual irregularities with Jadelle*

Complications	N=240	%
Irregular vaginal bleeding	62	24
Amenorrhea	42	16
Prolonged heavy bleeding	104	40
Prolonged spotting	52	20

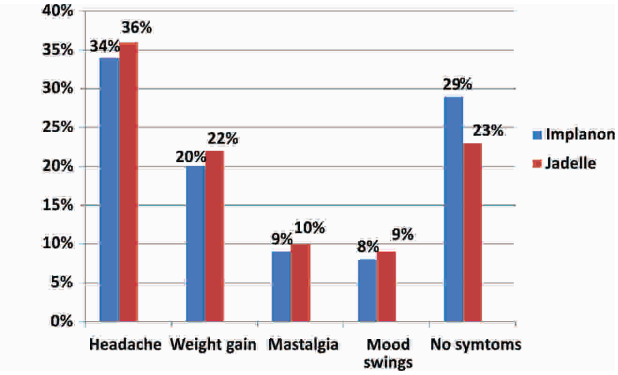
Table 10: *Adverse Effects other than Menstruation with Jadelle*

Adverse effects	N=240	%
Headache	94	36
Weight gain	57	22
Mood swings	26	10
Mastalgia	23	9
No Symptoms	60	23

around the world but the prevasiveness of use remains low. Contemplating that even the surgical method of female sterilization has a prevalence of use of 18% worldwide, and even as high as 36% in India,[6] implants have been slow to take off.[7] For



example, in France, only 2.6% of women younger



than 30 years were using an implant in 2010.[7] In Great Britain, in 2008, 1%–2% of women of child-bearing age were using the implant[8] Short-term and permanent methods are the most common contraceptive methods used in Pakistan, while the use of long-acting and reversible methods like IUDs and implants is only 2.3% and 0.1%, respectively.[9]

Current population of Pakistan is 201million and will be 310 million by year 2050. By Population Pakistan rank 6th country in world, 4th among Asian countries and 2nd in Muslim countries.[10]

Family planning services first started in 1953 in private sector then introduced to public hospitals in 1960. Contraception prevalence rate in Pakistan estimated to be 35% now on decline. According to FPP 2020(Global partnership for family planning) Pakistan aimed at to increase contraception rate up to 50%.[11]

The present study was conducted to evaluate sub dermal contraceptive implants for their acceptability, efficacy and safety in Jinnah hospital Lahore. Implanon insertions done in Jan 2015-Dec2016 were 312.

50(16%) women were younger than 20years. More than half of participants 190(60.8%) belonged to age group between 20-30 years and 72(23%) patients were more than 40 years. 176(28.8%) clients were P1-2. 357participants were having 3-4 kids making 58.3% of total and only 79(12%) had kids 5 or above. 60%of women opting for Implanon had cesarean section and 40% had vaginal delivery.

Approximately 67% of women were already practicing contraception. Condom use observed in 169 (27.6%) of users, 96(15.7%) were IUD users, 84(13.7%) had injections and 61(10%) were pill users. 33% of them not practicing any contraception. A study carried out at Nigeria by V.C.Pam and J.A. Karishma showed 80% of patients were practicing contraception previously. 50% of Nigerian women had used injectable contraception and 10-20% of them had used sub dermal implant previously. While only 10% of our women were using injectable contraceptives and none of them had exposure to sub dermal implant previously.[12]

Women with implanon were followed for 3 years. Initial follow ups done at 1st, 6th and 12th week of insertion then at 6th and 12th month or according to their complaints. 72 (23%) lost Follow up and 240(77%) women followed till end of study. Irregular cycles were most common and experienced by 65(27%) of women, followed by prolonged heavy bleeding in 48(20%) and prolonged vaginal spotting in 43(18%). 36(15%) women had amenorrhea while 48(20%) had no complaint regarding cycle. Gazginck et al reported less incidence of irregular bleeding(17.5%) but amenorrhea was common upto 41.5% with implanon.[13] According to a local study carried out by Abid S and Iqbal N amenorrhea was most common complaint 44%, followed by irregular periods 28%. Prolonged heavy periods and normal cycle experienced by 13.5% and 13.3% respectively.[14] Results of 11 clinical trial done on Implanon insertion in 923 patients showed that regarding bleeding problems irregular bleeding was most common 33.6%, followed by amenorrhea 22.3% and prolonged heavy cycles in 17.7%.[15]

Most common adverse effect observed in our study was headache, reported in 81(34%) of patients. Weight gain upto 5 kg at end of 12 months seen in 48(20%) of patients. Breast tenderness was present in 22(9%) and mood swings affected 19(8%). However 70(29%) women were symptom free. Brache et al reported incidence of headache upto 30% in implanon users and weight gain up to 1.5 kg / year in 22% which is comparable to our study.[16] Local study carried out at SIMS reported weight gain in only 7.8% and Mood changes in 9.8% of implant user which is comparable to our study.[17] Breast pain reported in 22% by Iqbal N.[14]

Implanon was found highly acceptable by users 86% of users continued it. Only 12(14%) requested removal due to complications. Out of 12 removals which were done due to side effect, most common were bleeding problems accounting for more than half removal i.e up to 6 removals. Second most common reason for removal was intractable headache and 4 removals were done due to this. 2 were removed due to persistent raised B.P. Pushpa B had shown removal in 37% cases. All of these were due to menstrual problem. No removal was done for adverse effects other then menstruation.[18]

No insertion or removal complications occurred in our study. Injury to ante brachial cutaneous nerve during removal and to ulnar nerve during insertion has been reported by Wechselberger et al and Osman et al respectively.[19,20] Spontaneous snapping of Implanon in two halves in situ at 33 months has been reported by Agarwal and Robinson.[21]

Implanon was not available after 2016 in our hospital. Since 2017 we are using Jedelle at our setup so long term experience with jedelle is not available at Jinnah hospital Lahore. Total 300 insertions had been done during 18 months. 260 patients are in follow up. 40% of patients reported prolonged heavy cycles after insertion of Jadelle. 24% had irregular cycle. 20% were having prolonged spotting. In comparison to implanon bleeding complications were more with jadelle. Almost all patients were having menstrual abnormalities and prolonged heavy bleeding was worrisome for patients while only 20% of patients were having this problem with implanon. However no removal is done due to this. There were no differences in adverse effects other then menstruation like headache, weight gain, breast pain, mood swings by both implants. They were almost same. Contrary to our study, research carried out on use of Jadelle in Thai and Nigerian women showed that commonest menstrual problem was amenorrhea reported 44% and 41% respectively.[22]

Satisfying the unmet need for modern contraception in developing countries would further prevent 54 million unintended pregnancies, including 21 million unplanned births, 26 million abortions (of which 16 million would be unsafe), and 7 million miscarriages; this would also help to prevent 1.1 million infant deaths. Globally, 56% of women use a modern method of contraception. However, the worldwide implant-prevalence rate is extremely low, at 0.3%.[23] If only 4% of current oral contraceptive users (100,000 women) in Pakistan switched to IUDs or implants, it is estimated that more than 25,000 unintended pregnancies could be averted over 5 years.[24]

CONCLUSION

In our setup patient's satisfaction rate was found to be less with jadelle.60% patients accepted bleeding problems but 40% found them difficult to

complete the tenure of 5 years. Rendering to its easy insertion and removal and fewer side effects Implanon found to be most effective and acceptable contraceptive method among women attending family planning clinic at Jinnah hospital Lahore. Proper pre insertion counseling can help to reduce the anxiety related with adverse effects and increase the acceptance by users. It is needed to follow women with jedelle insertion further to see its impact in our users. It would be more suitable for patients requiring long term effective contraception like patients with recurrent cesarean sections, hysterotomies , ruptured uterus with maternal morbidity for whom permanent methods for contraception are not suitable due to bad obstetric history.

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FREQUENCY AND REASONS FOR DELAYED HIV MEDICAL CARE

Nisar Haider Anjum, Sana Musaddiq, Nadeem Hussain, Amtiaz Ahmed, Saima Nouman Khan , Sana Iqbal Bokhari, Asma Azhar, Sobia Chaudhary

Abstract

Background: Acquired Immunodeficiency syndrome (AIDS) secondary to human immunodeficiency virus (HIV) infection is one of the major infectious epidemics faced by the world today. Highly active antiretroviral therapy (HAART) has reduced HIV-related morbidity and mortality but people still hesitate to get themselves registered with treatment centers because of many social issues. No local study have been conducted to find out reasons of delay in patients infected with human immunodeficiency virus in our population.

Objective: To determine the frequency of reasons of delay in initiation of treatment after diagnosis of HIV among patients infected with human immunodeficiency virus presenting to a tertiary care hospital.

Study Design: Cross Sectional survey

Study Setting: HIV Clinic. Jinnah Hospital, Lahore

Study Duration: Study was completed in Six months from 19th August 2015 to 18th February 2016.

Subjects & Methods: 385 patients infected with human immunodeficiency virus with prior diagnosis were enrolled ensuring confidentiality. Reasons of delay included: Didn't want to think about being HIV-positive, Felt good, didn't need to go, difficulties finding/accessing care, didn't believe HIV test result, didn't want to discuss HIV result.

Results: 385 patients with mean age of 31.08 ± 4.9 ranged from 19 to 37 years were included. 81 patients (21%) were female and remaining 304 patients (79%) were male. 68 patients (17.7%) had delayed treatment for more than 12 months after being diagnosed. 159 patients (41.3%) didn't want to think about being HIV positive. 159 patients (41.3%) felt well as reason for delaying the treatment. 301 (78.2%) delayed because they found difficulty in assessing care. 349 patients (90.6%) did not believe HIV test results and so many patients 349 patients (90.6%) did not want to discuss it.

Conclusion: It is concluded that the common reasons include did not believe HIV test and did not want to discuss. These may be used to modify the response of patients by health education and health protection strategies.

Keywords: Human immunodeficiency virus, Delay in initiation of treatment, HAART, Acquired immunodeficiency syndrome

Acquired Immunodeficiency syndrome (AIDS) secondary to human immunodeficiency virus (HIV) infection is one of the major infectious epidemics faced by the world today. 34 million people were affected by the year 2010 and total deaths of 1.8 million in the year 2010.[1-4] Pakistan is among the countries with established and expanding HIV epidemic[3,4] with an estimated prevalence of 0.1 %. [3] Currently 98,000 people are living with HIV by the end of 2009, with 5,256 PLHIV registered in 17 Anti retro viral treatment (ART) centers by end of 2011, including 189 children, 1,018 and 4,049 adult females and males, respectively.[4]

Highly active antiretroviral therapy (HAART) has reduced HIV-related morbidity and mortality but people still hesitate to get themselves registered with treatment centers because of many social issues.[5] These reasons vary from region to region. An early presentation for standard medical care has well-established benefits and better quality of life after start of treatment. 6,7 In a study 23% had delayed care entry greater than three months after diagnosis.

Reasons include: Didn't want to think about being HIV-positive. (n = 61/133, 45%), Felt good, didn't need to go (n=37/133, 27.8%), difficulties finding/accessing care (n=17/133, 12.8%), didn't believe HIV test result (n=19/133, 14.3%), didn't want to discuss HIV result (n=15/133, 11.3%).[6] In another study, ethnicity was found significantly associated with early or delayed presentation of HIV patient for treatment.[7]

The rationale of this study is that there is no local study available regarding reasons associated with delayed entry into primary HIV medical care after HIV diagnosis for Pakistani population. Ethnicity and local treatment seeking behaviors differ from other populations. Current study will help determine the reasons for delayed treatment after diagnosis among Pakistani HIV patient and help device some guidelines to reduce morbidity and mortality.

OBJECTIVE

Objective of this study was to determine the frequency of reasons of delay in initiation of treatment after diagnosis of HIV among patients infected with human immunodeficiency virus presenting to a tertiary care hospital.

Patient With Human Immunodeficiency Virus (HIV): Patients with detected HIV RNA detected by Polymerase Chain Reaction by a standard reference laboratory.

Delay In Initiation Of Treatment: It was labeled if there was delay in seeking treatment (coming to treatment care facility) more than three months of positive test results

Reasons For Delay In Treatment:

These included; didn't want to think about being HIV-positive, felt good AND didn't require medical care, difficulties finding/accessing care, didn't believe HIV test result and didn't want to discuss HIV result. Answers were dichotomous as yes or no and were asked at the time of inclusion into study.

METHODS

A Cross Sectional survey was conducted at HIV Clinic. Jinnah Hospital, Lahore from August 2015 18th February 2016. 385 subjects of age ranging from 18 to 60 years of either gender of HIV determined by HIV RNA detected by PCR were selected through a Consecutive, non-probability sampling after taking proportion of reason of delay 11.3% (least among all) among patients with human immunodeficiency virus and acceptable difference of 5%, and 95% confidence level. Patients not consenting, taking antiretroviral treatment or advice after diagnosis from private clinic determined by history and clinical records were excluded from the study. All variables of interest like identity (name was not recorded because of NATIONAL AIDS CONTROL PROGRAM GUIDELINES), age, gender, duration of delay in months along with reasons of delay were recorded on a standard questionnaire (attached as appendix I). Delay since diagnosis in months, education, socioeconomic status, was recorded additionally to cater effect modification. Data collected was entered and analyzed in the SPSS version 17. Mean with standard deviation was calculated for quantitative variables like age and delay in presentation. Frequency and percentages in case of categorical variables like gender, education and factors for delay as per operational definition. Data was stratified by age, gender, Delay since diagnosis in months, education, socioeconomic status to determine the effect modification. Chi square test was used post stratification. A p value < 0.05 was taken as significant.

RESULTS

385 patients were included with mean age of 31.08 ± 4.916 ranged from 19 to 37 years of age. 292 patients (75.8%) were more than 30 years whereas 93 patients (24.2%) were either 30 years or less in age. 81 patients (21%) were female and remaining 304 patients (79%) were male. 68 patients (17.7%) had delayed more than 12 months after being diagnosed. 65 patients (16.9%) had income high, 87 (22.6%) had middle and rest of 233 patients (60.5%) had low income status. Education of 258 patients (67%) was either metric or above and remaining 127 (33%) was below/under matric. (Table 1).

159 patients (41.3%) didn't want to think about being HIV positive. 159 patients (41.3%) did not felt good for delaying the procedure. 301 (78.2%) delayed because they find difficulty in assessing care. 349 patients (90.6%) did not believe HIV test results. 349 patients (90.6%) did not want to discuss it. (Table 2).

Cross tabulation of age group with reasons of delay i.e. did not want to think, felt good, Difficulty in assessing care, not believe test result and did not

want to discuss, the results came up significant on applying Fisher's exact test (p=0.001) that showed unequal distribution between both age group. (Table 3). When we Cross tabulated gender with reasons of delay i.e. did not want to think, felt good, Difficulty in assessing care, Did not believe test result and did not want to discuss, the results came up statistically significant on applying either Pearson chi square test or Fisher's exact test (p=0.001) that showed unequal distribution between both male and female patients. (Table 4).

When we Cross tabulated income with reasons of delay i.e. did not want to think, felt good, Difficulty in assessing care, Did not believe test result and did not want to discuss, the results came up statistically non-significant for did not want to think and felt good with p value 0.062 whereas in rest of the reasons results were significant (p<0.05). (Table 5)

DISCUSSION

Pakistan's HIV epidemic is fully established and expanding among injection drug users (IDUs) and their sexual contacts including male, female sex workers and transgender sex workers (MSWs)[2,3] similar is the case with diabetic epidemic which is on rise due to changing dietary habits.[4] There is a significant difference among developed and developing countries regarding momentum of both epidemics.[5]

An early presentation for standard medical care has well-established benefits and better quality of life after start of treatment.[6,7] The rationale of this study was that there is no local study available regarding reasons associated with delayed entry into primary HIV medical care after HIV diagnosis for Pakistani population. Ethnicity and local treatment seeking behaviors differ from other populations. Current study may help determine the reasons for delayed treatment after diagnosis among Pakistani HIV patient and help device some guidelines to reduce morbidity and mortality.

In our study, 68 patients (17.7%) had delayed more than 12 months after being diagnosed. Our results matches those reported in a previous study in which 23% of sampled population had delayed care entry more than 6 months.[6]

The reasons when ascertained, we got responses for five different reasons like Didn't want to think about being HIV-positive, delay "felt good", difficulties finding/accessing care (if center is away > 5km, no self-conveyance) , didn't believe HIV test result and didn't want to discuss HIV result. Reasons of delayed presentation were: 159 patients (41.3%) didn't want to think about being HIV positive, 159

Table 1: *Demographic Profile of Respondents*

Variables n=110	Frequency	Percentage
Age Mean =42.95SD=9.9		
> 30 years	292	75.8
< 30 years	93	24.2
Gender		
Male	81	21.0
Female	304	79.0
Income status		
High	65	16.9
Middle	87	22.6
Low	233	60.5
Education		
Matric	258	67.0
Under matric	127	33.0

Table 2: *Delay and Patients Perception*

Variables n=110	Frequency	Percentage
Delay > 12 months		
Yes	68	17.7
No	317	82.3
Did not want to think		
Yes	159	41.3
No	226	58.7
Felt good		
Yes	159	41.3
No	226	58.7
Difficulty in assessing care		
Yes	301	78.2
No	84	21.8
Did not believe test result		
Yes	349	90.6
No	36	9.4
Did not want to discuss		
Yes	349	90.6
No	36	9.4

Table 3: *Age and Reasons for Delay Cross Tabulation*

Variables n=385		Age Groups		Total	P values
		Less than 30 Years	More than 30 Years		
Did not want to think	Yes	0	159	159	P = 0.001
	No	93	153	226	
Felt good	Yes	0	159	159	P = 0.001
	No	93	153	226	
Difficulty in assessing care	Yes	57	224	301	P = 0.005
	No	36	48	84	
Did not believe test result	Yes	93	256	349	P = 0.000
	No	0	36	36	
Did not want to discuss	Yes	93	256	349	P = 0.001
	No	0	36	36	

Table 4: Gender and Reasons for Delay Cross Tabulation

Variables n=385		Gender		Total	P values
		Male	Female		
Did not want to think	Yes	110	49	159	P = 0.001
	No	194	32	226	
Felt good	Yes	119	49	159	P = 0.001
	No	194	32	226	
Difficulty in assessing care	Yes	220	81	301	P = 0.001
	No	84	0	84	
Did not believe test result	Yes	268	81	349	P = 0.001
	No	36	0	36	
Did not want to discuss	Yes	268	81	349	P = 0.001
	No	36	0	36	

Table 5: Income Status and Reasons for Delay Cross Tabulation

Variables n=385		Income status			Total	P values
		Low	Middle	High		
Did not want to think	Yes	93	31	35	159	P = 0.062
	No	140	56	30	226	
Felt good	Yes	93	31	35	159	P = 0.062
	No	140	56	30	226	
Difficulty in assessing care	Yes	191	66	44	301	P = 0.040
	No	32	21	21	84	
Did not believe test result	Yes	212	84	53	349	P = 0.007
	No	21	3	12	36	
Did not want to discuss	Yes	212	84	53	349	P = 0.007
	No	21	3	12	36	

patients (41.3%) felt good, 301 (78.2%) delayed because they find difficulty in assessing care, 349 patients (90.6%) did not believe HIV test results and 349 patients (90.6%) did not want to discuss it.

These results are comparable with the previous study. The study revealed: Didn't want to think about being HIV-positive (45%), Felt good, didn't need to go (27.8%), difficulties finding/accessing care (12.8%), didn't believe HIV test result (14.3%), didn't want to discuss HIV result (11.3%).[6]

Mean age of our sampled population came about 31.08 ± 4.9 ranged from 19 to 37 years of age. 292 patients (75.8%) in our study population were more than 30 years whereas 93 patients (24.2%) were either 30 years or less in age. This younger distribution of sampled population is alarming i.e. if not controlled now may lead to an explosion and may result in epidemic.

81 patients (21%) were female and remaining 304 patients (79%) were male. More male in our sample may be due to treatment seeking behavior of our population. Female are shy and less likely to present early with such a diagnosis. When we Cross tabulated gender with reasons of delay i.e. did not want to think, felt good, Difficulty in assessing care, Did not believe test result and did not want to discuss, the results came up statistically significant on applying either Pearson chi square test or Fisher's exact test (p=0.001) that showed unequal distribution between both male and female patients.

CONCLUSION

It is concluded that the common reasons include did not believe HIV test and did not want to discuss. These may be used to modify the response of patients by health education and health protection strategies.

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MANAGEMENT AND OUTCOME OF PATIENTS WITH NECROTIZING FASCITIS IN JINNAH HOSPITAL LAHORE

Zakir M, Abbas T, Salamat N

Department of Surgery, Jinnah Hospital Lahore

Abstract

Objective of Study: To find out presentation, management, Andoutcome of Synergistic Gangrene.

Study Design: Descriptive case series

Place and Duration of Study: Surgical unit 2 in Jinnah Hospital Lahore from 1st October 2016 to 2nd November 2018.

Methodology: Patients presenting with signs and symptoms were of synergistic gangrene included. Diagnosis was established on clinical assessment depending on the severity of illness. Aggressive treatment initiated which included antibiotics, fluidresuscitation, and oxygenation. Data recorded was statistically analyzed.

Results: Total fifty five patients were included in this study .There were forty two males and thirteen females so male to female ratio was 3:1.The age of the patient range from 35 -70 years. Forty seven patients were diabetics, forty patients had BMI > twenty five .Out of these 8 patients had BMI>forty five. Only 5 patients had BMI <eighteen. Other than diabetes mellitus there was no other co-morbidity seen. Eight patients had history of intramuscular injection in gluteal region which led to the synergistic gangrene. Thirty eight patients had involvement of scrotum, medial side of thigh including scrotum and partial denuding of penis. Six patients had isolated involvement of anterior abdominal wall with sparing the perineum. Eight patients who involved the gluteal region exposing the gluteal muscles, out of those one of them invaded the hip joint cavity. Two patients had involved upper limb one had history of intramuscular injection and other had trauma to upper limb by iron rod. At the time of presentation eighteen patients had mild sepsis twenty seven patients had moderate sepsis and ten patients had severe septic shock requiring intensive resuscitation.

Conclusion: Synergistic gangrene is a serious infective inflammatory disease with high mortality and morbidity. Awareness of personal hygiene especially in immunocompromised patients and teaching of standard skill of intramuscular injection to the paramedics.

Key word: synergistic gangrene outcome

Necrotizing fasciitis is a challenging fulminating necrotizing inflammatory condition of fascia with secondary necrosis of subcutaneous tissues. Necrotizing fasciitis affects about 0.4 in every 100,000 people per year in the United States[1]. It has been given other terms like Fournier's gangrene, acute dermal gangrene, Maloney's gangrene, hospital gangrene and synergistic necrotizing cellulitis. Generally, it is defined as rapidly progressing necrotizing process accompanied with severe systemic toxicity.[2,3] Necrotizing infection may involve any or all layers of skin and underlying tissues like dermis, subcutaneous fat and muscles. Process of necrosis may invade into nearby viscera as well. The incidence of this disease is increasing due to diabetes mellitus, immunosuppression, malignancies, I.V drug abusers, overcrowding and poor hygiene. Correct diagnosis and treatment include early surgical intervention and strong antibiotics.

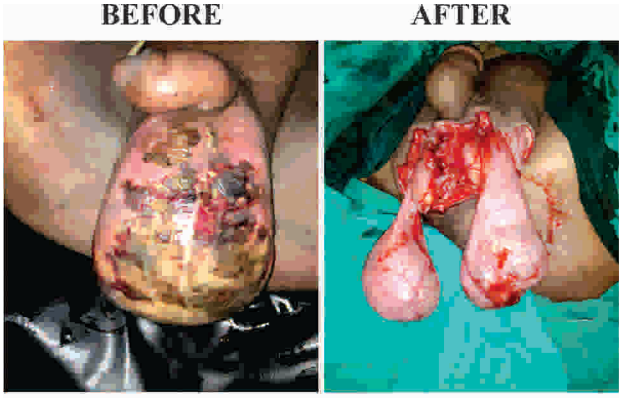
The main outcome of research for the presenting study is morbidity, hospital stay and mortality. The usual predictors of outcome in such illnesses are time of onset of illness in presentation to hospital, general conditions of patient and co-morbidities. The most important factor determining the outcome is the assessment of patient at the time of first presentation and categorization according to Fournier's

gangrene severity index. Patient with low severity index can be managed with the antibiotics, outdoor debridement and home dressings but patient with high severity index need isolation in HDU/ ICU. Due to severe systemic response to septic load, the patient need oxygenation, ventilation, central venous catheterization, measurements of venous pressure, monitoring of urine output, correction of electrolyte and acid base disturbances with some times inotropic supports. In this presenting study along with the care of co-morbidity, repetitive debridement, dressing and diversion of urine and feces was done. Great emphasis was made and carried out on above mentioned protocols in ICU and HDU. At field, great importance of special group of interest of doctors in various surveillance in surgical disorders and our team recreated a team added by consultants and few general surgical residents along with dedicated nurses and para medics. The team are responsible for the prompt response and on time debridement, washing and dressings.[4]

MATERIAL AND METHOD (Observational Study):

This study was carried out in surgical-2 Jinnah Hospital/ A llama Iqbal Medical College, Lahore from 1.7.2015 to 31.10. 2017. Patients presenting with signs and symptoms of soft tissue infections were included. Detailed history was taken to know the precipitating cause like trauma, I/M injection, diabetes mellitus, Immunosuppression and I V drug abuse. In clinical examination general severity of sepsis was assessed with level of consciousness. Pulse, respiratory rate, body temperature, blood pressure and volume of urine output. Further examination included site, extent, and depth of the necrotizing process with bullae and sign of crepitus. In case of frank discharge, discharge was taken for culture and sensitivity both aerobic and anaerobic. In other patients with insignificant discharge a suitable sized wet piece of necrotic tissue was taken for microbiological examination.

Debridement was done under suitable anesthesia on standard principle of surgery. Wounds were thoroughly irrigated with saline and padded dressing was done. Debridement and dressing continued till wound became healthy and granulated. Postoperatively, patients were looked after in general postoperative ward, HDU or ICU. Final covering was done with secondary suturing, superficial skin grafting or with different types of flaps with the help of plastic surgeon.



Fournier's Gangrene

MANAGEMENT:

Justified and correct use of antibiotic is also a factor leading to good outcome. Culture sensitivity reports should be followed promptly and the most sensitive antibiotic of correct dose helps in the brisk recovery. Patients and their family should be motivated to fulfill the nutrition of patient as these patients are severely catabolic. High calories with protein is another factor in good outcome of this severe septic disorder.

In all patients at the time of admission, assessment of severity of sepsis was done according to BUNDLE OF SHOCK which include clinical examination, pulse rate, urine output, mean arterial pressure, SPO2, BSR Monitoring, WBCs count and CRP.

1. Debridement in 10 patients.
2. Debridement and secondary suturing in 31 patients.
3. Debridement and flap replacement in 8 patients.
4. Debridement and burring of testis in 18

patients.

5. Debridement and colostomy in 03 patients.
6. Debridement and suprapubic cyst ostomy in 01 patient.

RESULTS

There were fifty five patients with synergistic gangrene admitted in surgical unit II from 01-10-2016 to 02-11-2018 (Figure 1). There were forty two males and thirteen females so male to female ratio was 3:1. The age of the patient range from 35-70 years. Forty seven patients were diabetic, forty patients had BMI > 25. Out of these eight patients had BMI > 45. Only five patients had BMI < 18. Other than diabetes mellitus there was no other co-morbidity seen in these patients. Eight patients had history of intramuscular injection in gluteal region which led to the synergistic gangrene.

Thirty eight patients had involvement of scrotum, medial side of thigh including scrotum and partial denuding of penis. Six patients had isolated involvement of anterior abdominal wall with sparing the perineum. 8 patients who involved the gluteal area exposing the gluteal muscles, out of those one of them invaded the hip joint cavity. Two patients had involvement of upper limb.

Demographic And Clinical Characteristics of Patients Undergoing Research of Fournier Gangrene

Sr.#	Parameter	Total Patients
1.	Mean Age (35-70)	
2.		
I	Diabetes	47
II	HCV	04
III	Alcoholic	01
IV	Smoker	13
V	HTN	12
VI	CKD	01
VII	IHD	04
VIII	CVA	02
IX	Hakeem Medication	03
3.	Fournier gangrene severity index	
I	+1	10
II	+2	10
III	+3	02
IV	+6	03

Figure 1

Mild Eighteen patients

Moderate Twenty seven patients

Sever septic shock Ten patients

Outcome of Patient During Hospital Stay

Sr.#	Parameter	Total Patients
1.	Mean Hospital Stay	7 days
2.	Morbidity	3
I	In the form of dissolution of testis	1
II	Fecal Fistula	1
III	Urinary Fistula	1
3.	Mortality	4

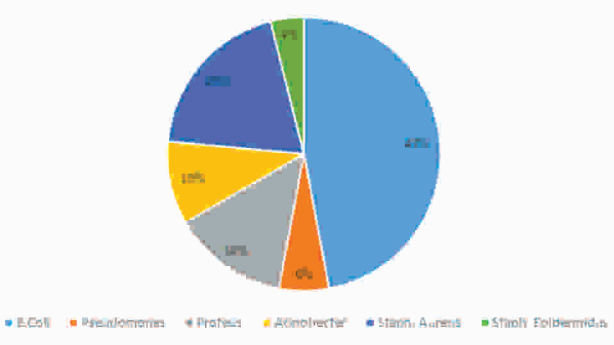


Figure 2

BACTERIOLOGY

Figure 3

DISCUSSION:

Necrotizing fasciitis is a challenging fulminating necrotizing inflammatory condition of fascia with secondary necrosis of subcutaneous tissues. Necrotizing fasciitis affects about 0.4 in every 100,000 people per year in the United States.[1] It has been given other terms like Fournier's gangrene, acute dermal gangrene, Maloney's gangrene and synergistic gangrene[5]. Synergistic gangrene is a disease of high mortality and morbidity.[6,7,8]

The incidence of disease is increasing due to diabetes mellitus, immunosuppression, malignancies, I V drug abusers, overcrowding and poor hygiene. The initiating events were scratching of genitals, trauma to the genitals, poor personal hygiene and some surgical procedures.[9]

The usual predictors of outcome in such illnesses are time of onset of illness in presentation to hospital, general condition of patient and co-morbidities. The most important factor determining the outcome is the assessment of patient at the time of first presentation and categorization according to Fournier's gangrene severity index.[10] But due to

changing concepts of inflammatory response this is difficult to apply now a days.

In this study at the time of admission, assessment of severity of sepsis was done according to BUNDLE OF SHOCK which include clinical examination, pulse rate, urine output ,mean arterial pressure, SPO2, BSR monitoring, WBC count and CRP.[11]

Patient with low severity index can be managed with antibiotics, outdoor debridement, home dressings, but patients with high severity index needs isolation in ICU. Due to severe systemic response to septic load, the patient needs oxygenation, ventilation. Central venous catheterization, measurement of venous pressure, monitoring of urine output, correction of electrolyte and acid base disturbances and sometimes with inotropic support.

Clinically, general severity of sepsis was assessed with level of consciousness. Pulse, respiratory rate, body temperature, blood pressure and volume of urine output. Further assessment included site, extent, depth of necrotizing process with bullae and signs of crepitus. In case of frank pus / discharge, discharge was taken for culture and sensitivity. In other patients with significant discharge a suitable sized wet piece of necrotic tissue was taken for microbiological examination.

The most common organism found in culture sensitivities is E.COLI in this study.[12]

The surgical management is aggressive resuscitation and debridement. Debridement was done under suitable anesthesia on standard principle of surgery. Wounds were thoroughly irrigated with saline and padded dressing was done. Debridement and dressings were done with normal saline and Edinburg University Solution of Lime (EUSOL). Debridement and dressings continued till wound become healthy and granulated.[13]

Final covering was achieved with secondary suturing, superficial skin grafting or with different types of flaps with the help of plastic surgeon.[14] Patients and their family were motivated to fulfill the nutrition of patients as these patients are severely catabolic. High calories with protein is another factor in good outcome of this severe septic disease.[15,16]

The incidence of this disease is increasing due to diabetes mellitus, immunosuppression, malignancies, I.V drug abusers, overcrowding and poor hygiene. Correct diagnosis and treatment include early surgical intervention and strong antibiotics.

CONCLUSION

Synergistic gangrene is a disease of poor outcome with high mortality and morbidity. But a structured care of such patient in initial assessment and categorization and severity of illness direct resuscitation, debridement, drainage, control of blood sugar level, care of nutrition can change the outcome of this severe septic disease.

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CHEST PAIN IN A PATIENT OF AORTIC ANEURYSM

Noor Dastgir[1], Naveed Iqbal[2], Arslan Masood, ZubairAkram[4]

[1]Assistant Professor, [2]Post Graduate Resident, [3]Associate Professor, [4]Professor

Department of Cardiology, Jinnah Hospital Lahore

Thoracic aortic aneurysm (TAA) represents approximately one-third of aortic aneurysm admissions.[1] Aortic aneurysm is one of the underlying causes of aortic dissection (AD), a dreadful complication. Incidence of aortic dissection is 5–30 cases per million inhabitants per year, having a high risk of mortality.[2] The classic symptoms of chest pain and other clinical signs of aortic dissection may mimic myocardial infarction and may lead to misdiagnosis and even diagnosis on postmortem examination.[3] Coronary malperfusion associated with aortic dissection is relatively rare, but when it occurs, it may have a fatal result for the patient. Up to 30% of patients suffering from AD are initially suspected of having other conditions.[3] Nevertheless, there are several reported cases of acute AD associated with electrocardiographic (ECG) signs of myocardial ischemia.[2-4] Coronary thrombosis can also coexist with aortic dissection[5]. Therefore when a patient with known aortic aneurysm presents with chest pain and an ECG sign of myocardial ischemia, it is crucial to rule out aortic dissection as a cause of myocardial ischemia as the treatment of two conditions differs markedly. The diagnosis of acute coronary syndrome (ACS) in this setting may lead to the inappropriate administration of thrombolytic or anticoagulant agents, resulting in catastrophic outcomes. [4-6]

CASE PRESENTATION

A 50-year-old male presented to the cardiac emergency with chest pain. The chest pain was central and crushing in nature. He was diaphoretic and experiencing nausea. Ecgdone, showed ST elevations in v1-v6 consistent with an acute anterior wall myocardial infarction. [Figure 1]

On further enquiry it was found that a previous echocardiogram done 3months back showed a huge aortic aneurysm. Under the circumstances, a strong clinical suspicion of aortic dissection arose and patient was thoroughly examined for signs of aortic dissection Including radio radial delay, radio-femoral delay and blood pressure differences in both arms, which however all proved inconclusive towards a diagnosis of aortic dissection. Transthoracic echo done in the ER also failed to show any dissection flap in the aorta [Figure 2]

Facilities of onsite Trans Esophageal Echo and CT-Angiogram were not available. The patient's symptoms soon started worsening and hence considering the anterior wall myocardial infarction and the clinical examination findings, the patient was infused with streptokinase (1.5 million units) over the next 1 hour. Patient's symptoms did not improve and he remained vitally unstable. CT-Angiogram [Figure 3] done the next day did however ultimately show an ascending aortic dissection (Stanford Type A) extending through the arch to the descending aorta. The patient ultimately expired the following day.

Figure 1

Correspondence: Arslan Masood F.C.P.S. , Assistant Professor of Cardiology,Allama Iqbal Medical College, Jinnah Hospital, Lahore, Pakistan Email: dr_arslanmasood@hotmail.com,

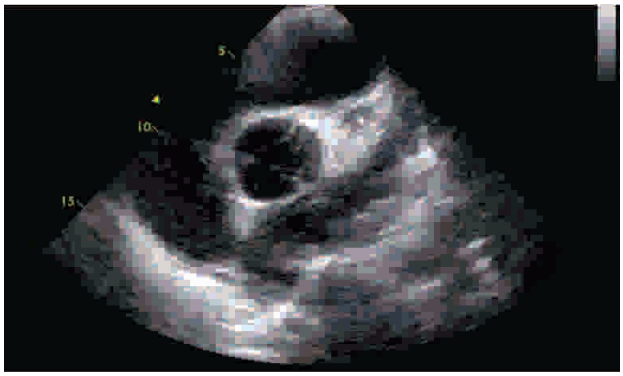

Figure 2

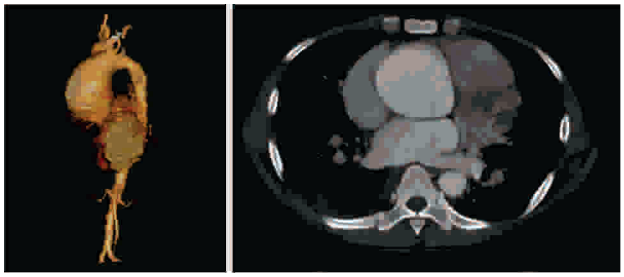

Figure 3

DISCUSSION

Chest pain in itself encompasses a wide spectrum of diseases. It must not be limited to acute coronary syndrome. Other diagnoses that masquerade as myocardial infarctions such as aortic dissection, myocarditis or pericarditis must always be considered in a patient presenting with chest pain, as standard management of infarction including thrombolysis may cause catastrophic results if the underlying disease was something else (maybe aortic dissection, as in our case). Clinical examination although sufficient in majority cases falls short by a considerable distance in this scenario. This highlights the necessity of high end equipment such as Transesophageal echo and / or CT- Angiogram as well as expertise in all centers dealing with cardiac emergencies. There have been previous reports as well of inappropriate administration of thrombolytics to patients of aortic dissection due to a missed diagnosis.[7,8]

The physician must ensure a delicate balance between offering treatment to those in whom it will help and withholding it from those whom it may harm. This report demonstrates the dangers of initiating thrombolytic therapy before the diagnosis is certain. The physician must ultimately first and foremost adhere to the caveat of "first, do no harm." By this case we want to alert emergency physicians to get CT angiogram/ Tranesophageal echo before instituting any further therapy in a patient with known aortic aneurysm who presents with chest pain and electrocardiographic changes of myocardial ischemia in whom clinical and echocardiographic signs of dissection are absent.

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GARLIC INDUCED SIGNIFICANT VASODILATATION, HEMORRHAGES AND CONGESTION IN THE HEPATIC MICROCIRCULATION IN ALBINO RATS.

Asma Siddique[1], Muhammad Suhail[2]

[1]Assistant Professor Anatomy, Akhtar Saeed Medical & Dental College Bahria Town, Lahore;
[2]Professor Head of Anatomy: Shaikh Zayed Post Graduate Medical Institute, Lahore & Shaikh Khalifa Bin Zayed Al-Nahyan Medical & Dental College, Lahore

Abstract

Background: Garlic has important dietary and medicinal value specially in the diabetic and hypertensive patients. It wide usage necessitates the importance to rule out its safer dose range and duration of consumption because it is not bioavailable and completely metabolized in the liver.

Aim: To evaluate the adverse effects of garlic (allium sativum) extracts on liver of adult albino rats.

Methods: In this experimental study a total of 45 wistar albino rats of both sexes weighing between 250-350 grams were selected randomly. Two different doses of 500 and 1000 mg/kg of fresh garlic extract by orogastric tube for thirty days were given to the animals. After this period histopathological analysis was then performed on the livers of the sacrificed rats.

Results: In the present study, histologically the sinusoidal congestion and hemorrhages were noted. Grossly dilated central vein with disrupted endothelial cells were also seen in all animals of experimental groups B and C as compared to control group A (P-value < 0.001).

Conclusion: It is concluded that there is a need to evaluate safer dose and duration of usage of garlic in general public due to its gross morphological destructive effects on liver. So its use as self medication should be avoided.

Keywords: Garlic (allium sativum), liver, congestion, sinusoids, central vein, albino rats

Garlic (Allium sativum) has very growing and widespread usage over the centuries. Sale of garlic as prescribed herbal drug was at highest rank in the Germany alone.[1] Allicin (allyl 2-propenethio-sulfinate or diallyl thiosulfinate) is thought to be the principal bioactive compound present in aqueous garlic extract or raw garlic homogenate. When garlic is chopped or crushed, allinase enzyme, present in garlic, is activated and acts on alliin (present in intact garlic) to produce allicin.[2] The efficacy of the garlic is well known as antihypertensive, hypoglycemic, hypolipidemic, antimicrobial and anticoagulant.[3] The mechanism of its protective role is due to its key role as an antioxidant to counteract the oxidative stress at the tissue level.[4]

On the other hand higher doses of garlic has toxic effects on the stomach, liver, kidneys, testis and blood vessels. Prolonged feeding at higher level was reported as the clastogenic in the mice (das et al 1996). Rats treated with 200 gm/l garlic extract for 10 days showed marked rise in hepatic enzymatic biochemistry like aspartate aminotransferase, liver lipase but decrease in catalase and superoxide dismutase indicating possible lethal oxidative stress.[5] In a study, hepatotoxic effects were noted due to dried garlic consumption to hyperlipidemic rats. It showed atrophy of hepatocytes with pyknosis of their nuclei and vacuolar degeneration along with inflammatory cell infiltration in the hepatocytes. Other features were marked thickening in the wall of bile duct, dilatation and congestion of hepatic sinusoid and significant cell injuries in the areas of portal triad. Ultrastructural study of hepatocytes showed disruption in normal cellular framework and loss of cellular organelles. Fatty change, swollen hepatocytes, damage to plasma membrane and

periportal necrotic areas were also noted.[6]

Garlic supplementation may enhance the risk of postoperative bleeding. Garlic intake might increase the effects of anticoagulants. Its potential interaction with aspirin and warfarin has been documented.[7] Garlic can lead to miscarriages and alteration in menstrual cycle. It has been proved utero-active with increased fetal movements during pregnancy.[8]

METHODS

This experimental study was conducted in Department of Anatomy, Shaikh Zayed Postgraduate Medical Institute, Lahore in collaboration with Department of Zoology Quaid-e-Azam Campus, University of the Punjab Lahore. 45 wistar albino rats of both sexes weighing between 250-350 grams were selected for this study. After 14 days of acclimatization the animals were randomly divided into three groups. Each group comprised of 15 animals. Group A was control, the animals of this group were not given garlic extracts but instead received distilled 4 ml/kg body weight of water by orogastric tube for 30 days. The other two groups B & C were experimental. Garlic extract 500 mg/kg and 1000 mg/kg was given respectively to the rats of experimental groups B & C through the orogastric tube for 30 days.

Garlic bulbs were purchased from the local market and then its extract was obtained from PCSIR, Laboratories Complex Lahore, which was prepared by soaking garlic paste in purified water. From 25 g of raw garlic, 1 ml of garlic extract was obtained which contained approximately 90 mg of allicin. Two concentrations of extract were prepared 0.2 and 0.3 g/ml corresponding to doses of 500 and 1000 mg/kg body weight of animals respectively.[5] At the end of study the rats of all groups were weighed properly before dissection and recorded in proforma. On the day 7 all the rats were euthanized by giving morphine 0.3–0.5 mg/kg intraperitoneally, as an analgesic agent. The anaesthetic agent sodium pentabarbitol was administered intraperitoneally with dose of 45 mg/kg.[9] After dissection the histologic parameters recorded were inflammation and congestion in the periportal areas.

Statistical analysis:

The qualitative data for inflammation and congestion in portal triad was reported by using frequency and percentage of each group. Comparison among groups was made by using Chi-square test. P-value < 0.05 was considered significant.

RESULTS

The gross appearance of livers of all the animals of experimental groups B and C showed haemorrhagic areas on external surface randomly affecting all lobes as compared to smooth surface of control group A.

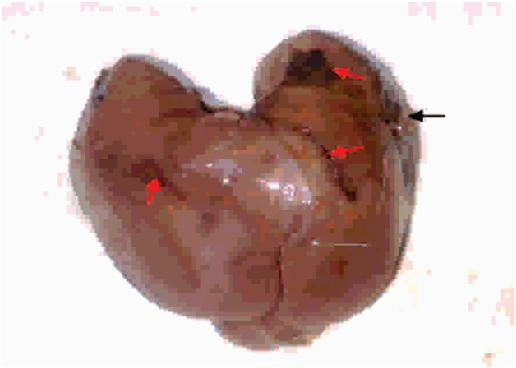

Fig:1 *Photograph Showing Gross Haemorrhagic Areas on External Surface of Liver of Albino Rats in Experimental Group C (Red Arrows) and Distorted Margins (Black Arrow).*

When observed it was seen that the hepatic sinusoids were congested and the central veins were grossly dilated in all (100%) animals of experimental groups B and C and normal in all animals of control group A (Fig. B, C & D). The difference was statistically significant (P-value < 0.001, Table 1) The group wise comparison revealed that the difference of the group B and C from group A was statistically significant (P-value < 0.001) and the difference between group B and C was statistically insignificant (P-value 1.000, Table 2). The shape of endothelial cells lining the central vein was normal showing simple squamous epithelium in all (100.0%) animals of group A and B. The experimen-

tal group C showed disruption and broken margins of endothelial cells with seepage of blood in the surrounding areas of the central vein. (Table 3, Fig. D) The difference among the groups was statistically significant (P-value < 0.001, Table 4).

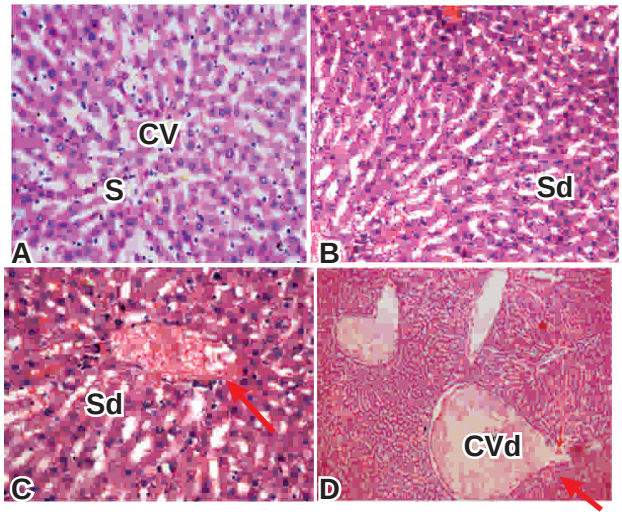

Fig:2 *Photomicrographs of Liver of Adult Albino Rat Of Control Group A And Experimental Groups B &D Showing Dilated Sinusoids (Sd) and Fig D Showing Dilated Central Vein (CVd) with Disrupted Endothe-Lial margins.(Red Arrows) (H & E)*

Table 1: *Congestion of Hepatic Sinusoids of Rats in Control and Experimental Groups after Administration of Garlic Extract*

GROUPS	NORMAL		CONGESTED		TOTAL	
	N	%	N	%	N	%
A	15	100.0	0	0.0	15	100.0
B	0	0.0	15	100.0	15	100.0
C	0	0.0	15	100.0	15	100.0

Chi-square = 45.0 p-value < 0.001
A Control Group B Experimental Group
C Experimental Group N Number of Animals

Table 2: *Comparison of Congestion in Hepatic Sinusoids of Rats in Control and Experimental Groups after Administration of Garlic Extract*

GROUP I	GROUP 2	CHI-SQUARE	DF	P-VALUE
Group A	Group B	26.0	1	< 0.001**
	Group C	26.0	1	< 0.001**
Group B	Group C	0.0	1	1.000++

A Control Group
B Experimental Group
C Experimental Group
DF Degree of freedom
** Highly significant difference (P < 0.01)
++ Non-significant difference (P > 0.05)

Table 3: *Shape of Endothelial Cells of Rats in Control And Experimental Groups After Administration of Garlic Extract*

GROUPS	NORMAL		DISRUPTED		TOTAL	
	N	%	N	%	N	%
Group A	15	100.0	0	0.0	15	100.0
Group B	15	100.0	0	0.0	15	100.0
Group C	0	0.0	15	100.0	15	100.0

Chi-square = 45.0 p-value < 0.001
A Control Group
B Experimental Group
C Experimental Group
N Number of Animals

Table 4: *Comparison of The Shape of Endothelial Cells of Rats in Control and Experimental Groups After Administration of Garlic Extract*

GROUP I	GROUP 2	CHI-SQUARE	DF	P-VALUE
Group A	Group B	0.0	1	1.000
	Group C	26.0	1	< 0.001**
Group B	Group C	26.0	1	< 0.001**

A Control Group
B Experimental Group
C Experimental Group
DF Degree of freedom
** Highly significant difference (P < 0.01)
++ Non-significant difference (P > 0.05)

DISCUSSION

Garlic has its most popular use in our daily diet. It has medicinal importance for its multiple beneficial and protective effects. It is also a fact that garlic has been taken for granted and considered as safer in wide range of doses. Recently it has been reported that it is toxic at higher doses especially when used chronically.

The present research work was designed to evaluate the harmful effects of garlic on morphological and histological parameters of liver as it is the main metabolizing organ for garlic and its constituents. The sulphated constituents of garlic impose cellular damage due to high oxidative stress.[10] Allicin is the most bioactive sulphated component that has been proved lethal.[11] In this present study toxic effects of garlic were observed in doses of 500 and 1000 mg/kg which was given for 30 days and the gross and histological effects on liver were observed. The complex functions of the liver in biosynthesis,

metabolism, clearance, and host defense are tightly dependent on an adequate microcirculation. To guarantee hepatic homeostasis, this requires not only a sufficient nutritive perfusion and oxygen supply, but also a balanced vasomotor control and an appropriate cell-cell communication.[12] The gross appearance of experimental group B and C showed hemorrhagic areas on external surface randomly affecting all lobes of liver in group B and C (Figs. 1). These results showed that by increasing the dose of garlic the haemorrhagic areas were also increased. It was possibly due to the vasodilator and antithrombotic effects of garlic.[13] Makheja and Bailey identified that antiplatelet components in allium vegetables like onion and garlic are adenosine, allicin and polysulfide. Adenosine and allicin both act as antiplatelet by inhibiting platelet aggregation. Antiplatelet mechanism of garlic constituents had no effect on the arachidonic acid metabolic pathway that produced cyclooxygenase and lipoxygenase metabolites.[14] These findings correlate with the study performed by Sainani who observed the effects of garlic as antithrombotic and increased fibrinolytic activity in rabbits by giving 250 mg/kg raw garlic juice.[15] A study performed by Ansari revealed fibrinolytic activity of blood clot in vitro.[16]

The hepatic sinusoids were congested in all (100.0 %) animals of experimental group B and C and normal in all animals of control group A (Figs.2 B & C). This showed statistically significant results (P-value <0.001, Table 1,2). Cytoplasmic vacuolization in hepatocytes and congestion in the hepatic sinusoids were observed by Rehman in a study in which the effects of dried garlic were seen in hyperlipidemic rats.[6]

In this present study, experimental groups B and C showed marked dilatation of central vein with increased diameter as compared to control group A (Fig.2D). When difference was observed pair wise, it was noted that the difference for all three groups was statistically significant (P-value < 0.001, Table 3,4). Garlic has potential vasodilator action and it modulate the production nitrous oxide which is one of endothelium derived relaxing factor. Nitrous oxide is capable of eliciting relaxation in blood vessels.[17] This is in accordance with the findings observed by Ebomoyi, who studied the effect of aqueous fresh garlic (Allium sativum) cloves extracts on liver and pancreas of wistar rats in dose of 500 mg/kg body weight. The results of his research showed that the vascular changes in the liver and the pancreas were associated with increased blood flow and caused dilatation.[18]

The shape of endothelial cells was normal in all (100.0%) animals of group A and B and disruption was seen in all animals of group C with significant results (P-value 0.001, Fig D). The toxic metabolites of garlic induced oxidative damage to endothelium lining of blood vessels. This is basically due to damaging effects in polyunsaturated fatty acids mainly present in the phospholipids components of the endothelial cell membranes.[19]

CONCLUSION

The use of garlic extract in high doses for longer time caused significant vasodilatation and congestion in liver of albino rats. It is worth noting that garlic is completely metabolized in liver and that is the main cause of its toxicity. The possible mechanism behind its damaging effect is oxidative stress at cellular level. Most lethal effect as indicated in this research work is significant central vein dilatation, hemorrhages and sinusoidal congestion. It must be kept in mind while prescribing garlic to hypertensive and diabetic patients because it is not safe as used in excess. There is a need to evaluate safer dose and duration of usage of garlic in general public. In a nutshell, it is worth noting that Garlic and its metabolites induce significant morphological and histological changes in the liver.

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AGREEMENT BETWEEN "SMOOTH MUSCLE MYOSIN HEAVY CHAIN" AND "SMOOTH MUSCLE ACTIN" FOR DIFFERENTIATION OF INVASIVE AND NON INVASIVE BREAST LESIONS IN TRUCUT BIOPSIES

Sara M Cheema[1], Rahat Sarfaraz[2], Muhammad Imran[3], Tazeen Anis[4], Sidra Munir[5], Sehar Iqbal, Noshin Wasim Yusuf[6]

[1]Senior Demonstrator Azra Nahid Medical College, [2]Associate Professor FJMU, [3]Assistant Professor AIMC, [4]Senior Demonstrator AIMC, [5]Mphil Trainee AIMC, [6]Professor RLMC Lahore

Abstract

BACKGROUND: Carcinoma of the breast is the commonest malignancy in females all over the world and second leading cause of death due to cancer among females. Differentiation of benign proliferative breast lesions and in situ form malignant invasive tumors is of paramount importance. In-situ carcinomas and benign epithelial proliferative lesions retain an intact peripheral layer of Myoepithelial cells (MECs) whereas this cell layer is lost in invasive carcinomas. In routine Hematoxylin and Eosin (H&E) stained sections diagnosis of several proliferative breast pathologies is difficult, since MECs may not be easily visible. This difficulty is augmented in tru-cut biopsies due to limited tissue sample. Here immunohistochemical markers like Smooth Muscle Myosin Heavy Chain (SMMHC) & Smooth Muscle Actin (SMA) play a pivotal role.

SUBJECT: The rationale of this study was that in a resource limited setting of our country we need to select the best possible immunomarker for routine diagnostic purposes. The study was designed to see the agreement between two markers used to highlight myoepithelial cells SMMHC and SMA for differentiation of benign from malignant breast lesions and carcinoma in-situ from invasive carcinomas in tru-cut biopsies. Traditionally SMMHC demonstrates less cross-reactivity to myofibroblasts than either SMA or other markers. The objective was to determine the degree of agreement between SMA and SMMHC for identifying MECs in invasive and non invasive breast lesions in trucut biopsy

METHODOLOGY: 75 cases of breast trucut biopsies were included in this study. After initial evaluation each case was stained for SMMHC & SMA.

RESULTS: KAPPA Statistics were applied to calculate agreement between these two markers in differentiating non invasive lesion from invasive lesions. A measure of agreement of 0.967 was obtained which is almost perfect agreement between the two markers.

CONCLUSION: This study concludes that there is near complete agreement between SMMHC & SMA. Therefore either one can be used as a myoepithelial cell marker in trucut biopsies in our resource limited setting. SMA nevertheless is a slightly more cumbersome stain to interpret subjectively as stromal myofibroblast staining can confound its interpretation. So we recommend SMMHC also as a marker suitable for myoepithelial cells.

Key words: Myoepithelial Cells, Smooth Muscle Myosin Heavy Chain, Smooth Muscle Actin, Invasive Breast Lesions, Non Invasive Breast Lesions, Trucut Biopsy, Degree of Agreement

Breast cancer is one of the most focused on cancers. Despite the successfully accomplished awareness campaigns & implemented screening protocols breast cancer is still the most frequently occurring cancer in women with an incidence of 29% by site and sex as per American cancer society cancer stats 2011.[1] It is a close second as far as mortality is concerned trailing at a 15%

behind the number one cancer killer – Lung cancer. In females alone it is the most common cause of cancer death.[2,1] 1.67 million new cases were diagnosed in 2012, constituting 25% of all cancers.[2]

Pakistan being a developing country is still struggling with the establishment of a nationwide cancer registry that can provide health care professionals and researchers with easily retrieved robust data. Nevertheless there is a treasure of concordant information regarding breast cancer burden in the country found in academic literature. It is documented to be the most common cancer in Pakistani females as reported from most regions.[3,4,5,6,7,8,9,10]

Breast diseases appear to develop along lines of a continuum; broadly categorized from non proliferative breast disease to proliferative breast disease without atypia (low risk) to proliferative breast disease with atypia (high risk) to carcinoma in situ to invasive carcinoma; with each step postulated by various authors to be a non obligate precursor to the next one.[11,12] Nevertheless accurate diagnosis of each is necessary as management for each differs.

The main distinction for management purposes is between an invasive and a non invasive lesion. This is the point of decision making between Lumpectomy with clear margin (breast conserving surgery) & mastectomy with sentinel lymph node biopsy / axillary lymph node dissection.

Internationally trucut biopsy has been replacing FNAC for preoperative assessment over the years.[13,14] In Pakistan as well trucut biopsy for breast lesions has gained popularity with a great increase in number of trucut biopsies being received over the past two decades.

Since the use of trucut biopsies has increased worldwide there is a wider variety of lesions presenting on trucut and more and more challenges are presented to the pathologist. It has been postulated that the main challenges for the pathologist are the reporting of intraductal proliferations, atypical lesions and especially accurate distinction of insitu cancer from invasive cancer.[13,15,16] In these cases the identification of MEC layer can markedly facilitate the diagnosis.[17,18,19,21] MEC are mostly visible on H&E staining but in a small biopsy specimen with the need for an accurate diagnosis it is prudent to highlight the MEC with immunohistochemical stains.[13,15,20,21,17,19] Mammary myoepithelial cells comprise the basal layer of the epithelium in the ducts & lobules of the mammary gland. These cells are strategically located between the luminal cells and basement membrane.[22,23] MECs are considered to be a nature barrier to tumor invasion, but their role in tumor inhibition is very complex and ever expan-ding as more properties of MECs are coming to light.[24,25,26]

Traditionally immunohistochemical markers for the identification of MECs have been categorized into three main groups.[17,27]

- Smooth muscle related: SMMHC, SMA, Calponin & H Caldesmon.
- Cytokeratins: includes CK5, CK10, CK14, CK 17 & the antibody 34βE12 which recognizes CK1, CK 5, CK 10 & CK 14.
- Other markers: these markers identify various properties or products of the myoepithelial cell. Some identify tumor suppressor proteins in MECs example include S100, CD10, P Cadherin, p 63, Mapsin, WT1, 14-3-3α & Mapsin.[17,21,28,20]

Each marker has its benefits & pitfalls. To date there is no single gold standard IHC marker for detection of MEC. Most authorities advocate the use of two or three markers in combination with one smooth muscle related marker preferred to be used in combination with another marker. Mostly the recommended combination is of SMMHC and p63[17,21,19,29,20]

The past one to two decades has seen a torrent of research and academic activities centered on the recently popularized myoepithelial cell. From Pakistan much data has been published in the past 10 to 20 years regarding breast lesions in which IHC has been used. Most of the original study works and reports have focused on prognostic marker in IDC and IHC based surrogate molecular subtyping.[30, 31, 32,

[33, 34, 35, 36, 4, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47] There is no research exclusive for myoepithelial cell markers or their comparisons. Pakistan literature indicates that the most commonly used marker for myopepithelial cell is SMA,[48,49,50] this is also the more commonly available and frequently used marker for myoepithelial cells in most labs even though data to support this is not reported. No research studies in Pakistan have used SMMHC.

International data also suggests that traditionally SMA is more frequently used although following evidence based recommendations SMMHC is becoming more popular.[13]

1986 Nagle RB et al[51] in Germany used K1 / CK5, KG 8.13 / CK 5 & K4 / CK 19 as MEC markers. Lazard D et al[52] in 1993 in France studied SMA, SMMHC, Calponin, h – Caldesmon & α1-Integrin. Yaziji H et al[18] of USA in 2000 studied various markers. In 2002 Moritani S et al[53] studied CD 10, SMA & S100. In 2003 Werling WR et al[54] studied P 63, SMMHC & Calponin. Castelluccia L & Milne AW[13] from UK in 2003 SMA, SMMHC, CK 5/6, Calponin & p63. Zhang RR et al[55] in 2003 studied SMA, Mapsin, Calponin, SMMHC, WT & CD 10. Man YG et al[56] in 2003 studied SMA. Stenfanou D et al[57] of Greece in 2004 applied P63, SMA, S100 & CK14. Hill CB &Yeh IT[15] in 2005 applied Calponin, SMMHC & p63. Jing HB (Phd thesis)[58] in 2006 worked on S100, SMA, Calponin, CD10 & P63. Savage K et al[59] in 2007 studied Caveolin1 as MEC marker. Tse GMK et al60 in 2007 applied SMA, p63, CD10 & CK14. In 2010 Hilson JB et al61 used SMA, Calponin , SMMHC, p63, CD10, CK 5/6 &. Ahmed Z.A. M (Msc dissertation) 62 in 2010 studied p63 as MEC marker. Bhatiya Y28 in 2013 studied P-Cadherin. Ahmed KO (PhD thesis)63 in 2014 studied galectin-7. Youssef NS & Hakin SA64 in 2014 studied Fascin & MMP 9. Russell TD et al65 in 2015 studied p63, Calponin & SMA in. In 2017 Yamamoto Y et al[66] performed a morphometric classification of MECs using machine learning approach, they also used p63 as MEC marker.

The academic narrative from Pakistani literature is sparse for this celebrated cell and the work done in our department is of significance for breast lesion diagnoses as well as a contribution to the pool of knowledge regarding phenotypic expression of the myoepithelial cell and is of significance especially as a contribution to Pakistani literature.

METHODOLOGY

SETTING: This study was conducted in Department of Pathology, Allama Iqbal Medical College, Lahore over a period of 6 months

STUDY DESIGN: Descriptive, cross sectional study

SAMPLE SIZE: Sample size of 75 cases was calculated with 95% confidence level, 7% margin of error and taking expected percentage of degree of agreement between SMA and SMMHC in the diagnosis of noninvasive vs. invasive breast lesions as 90%.

SAMPLE TECNIQUE: Non probability / consecutive sampling technique

INCLUSION CRITERIA: Specimen of trucut breast biopsy with suspected malignancy, Specimen with viable lesion.

EXCLUSION CRITERIA: 1) Autolyzed specimens determined by physical examination Specimen suboptimal fixed in formalin (within < 6hours) determined on microscopy, 2) Biopsy from breast abscess determined on microscopy & 3) Biopsy with suspected mastitis determined on microscopy.

SPECIMEN DEALING: This comprised grossing (measuring and counting the number of biopsies), processing, slide formation, H&E staining and then Immunohistochemistry. H&E stained slides were studied for making a diagnosis of benign, malignant or cases suspicious for invasive malignancy. After confirmation of the morphological diagnosis of the cases two sections were cut from each block, with 3 to 4 µm thickness One section was labeled to be stained with SMMHC and the second section was labeled to be stained with SMA. These sections were taken on poly-L-lysine coated slide or DAKO IHC microscope. Slides were fixed in oven at 58 to 60 0C

for 50 to 60 minutes.

All the cases were reacted with 1) Flex Monoclonal Mouse Anti Human Smooth Muscle Myosin Heavy Chain (Clone SMMS-1, Code ISO66) by Dako and 2) Flex Monoclonal Mouse Anti Human Smooth Muscle Actin (Clone 1A4, Code IS611) by Dako, following the manufacturer specified protocol

INTERPRETATION OF IMMUNOHISTOCHEMISTRY: SMA & SMMHC identifiy presence of myoepithelial cells as brown cytoplasmic staining. When myoepithelial cells were stained by SMA on immunohistochemistry it was recorded as a non invasive lesion. When myoepithelial cells were not stained by SMA on immunohistochemistry it was recorded as an invasive lesion (shown in the picture 6). SMMHC identifies presence of myoepithelial cells as brown cytoplasmic staining. When myoepithelial cells were stained by SMMHC on immunohistochemistry it was recorded as a non invasive lesion. When myoepithelial cells were not stained by SMMHC on immunohistochemistry it was recorded as an invasive lesion (shown in the picture 5).

The positivity was compared with that of positive control. Agreement was labeled when both SMMHC and SMA agreed upon diagnosis of invasive or non invasive lesion.

DATA ANALYSIS: Data was entered and analyzed in SPSS Ver: 17.0. Frequency and percentages were calculated for agreement. Cross tabulation was done between SMMHC and SMA for diagnosis of benign and malignant conditions and Kappa statistics were calculated for degree of agreement. P value ≤ 0.005 was taken significant.

RESULTS:

- Of a total of 75 cases included in the study 17 cases were of IDC, 11 of fibroadenoma, 8 of benign parenchyma, 5 of Phyllodes tumor, 5 of Tubular adenoma, 4 of Adenosis, 4 of Fibrocystic Change, 4 of Inconclusive diagnoses, 4 of UDH, 3 of DCIS, 2 of Atypical cells, 2 of IDC with DCIS, 2 of Papillary lesion, 2 of Sclerosing Adenosis, 1 of Adenoid Cystic Carcinoma, 1 of ALH, 1 of Columnar Cell Change & 1 of Traumatic fat necrosis. See Figure 1
- SMA labeled 28.0% Invasive and 72.0% non invasive, of these 41 were benign, 15 mixed, 11 insitu, 6 invasive & 2 papillary lesions. SMMHC labeled 29.3% Invasive and 70.7% non invasive of these 41 were benign, 12 mixed, 10 insitu, 10 invasive & 2 papillary lesions. See figures 2 & 3.
- KAPPA value of .967 was obtained. Therefore there was an almost perfect agreement between SMMHC & SMA within this study. See Table 1
- Additional findings regarding myoepithelial cell morphology, myofibroblast staining, breast lesion categories and staining characteristics for MECs in DCIS cases were observed and recorded. Details of these findings will follow in a subsequent publication.

Table: *Kappa Statistics*

		SMA		Total	
		Invasive	**Non Invasive**		
SMMHC	Invasive	21	1	22	X^2= 70.265 P = .000
		100.0%	1.9%	29.3%	
	Non Invasive	0	53	53	
		0.0%	98.1%	70.7%	
Total		21	54	75	
		100.0%	100.0%	100.0%	

Kappa Agreement

- < 0 Less than chance agreement
- 0.01–0.20 Slight agreement
- 0.21– 0.40 Fair agreement
- 0.41–0.60 Moderate agreement
- 0.61–0.80 Substantial agreement
- 0.81–0.99 Almost perfect agreement

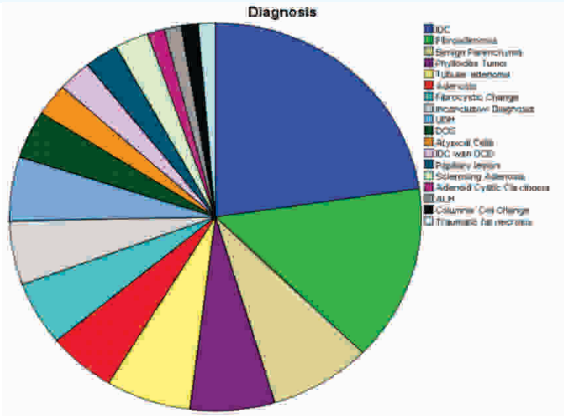


Figure 1 – *Pie Chart of Diagnoses*

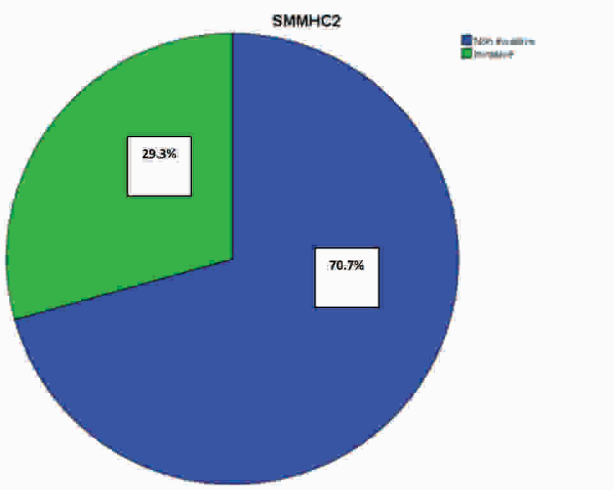


Figure 2 - *Pie Chart of Invasive & Non Invasive Lesion on SMMHC showing 29.3% Invasive and 70.7% Non Invasive*

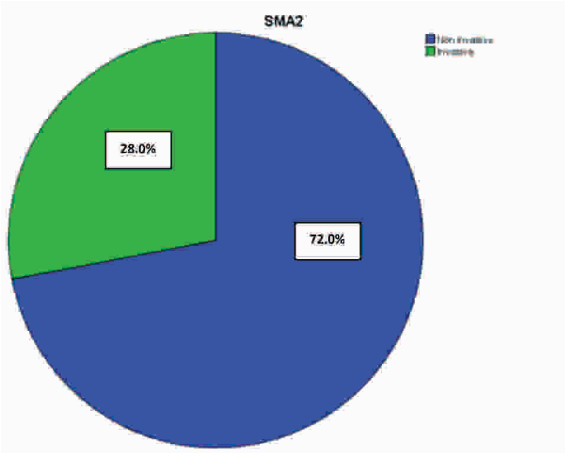
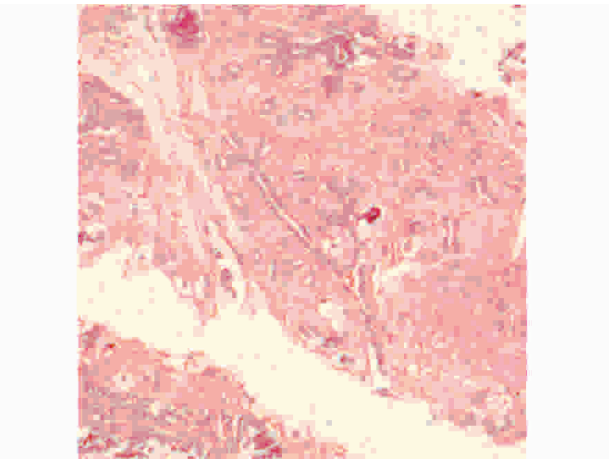
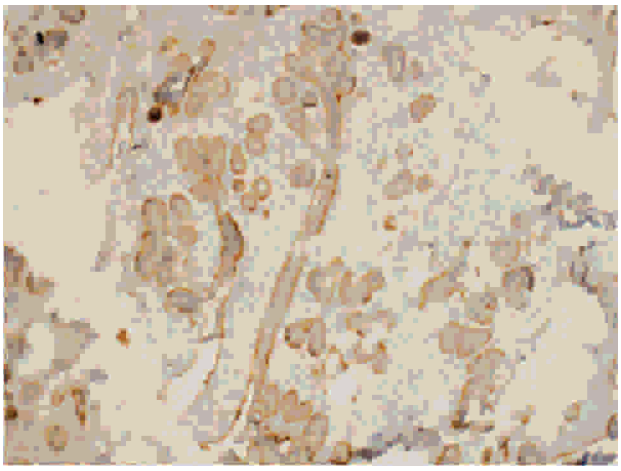


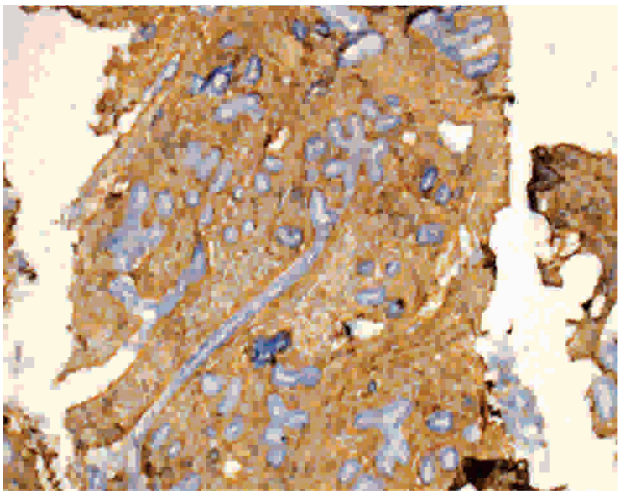
Figure 3- *Pie Chart of Invasive & Non Invasive Lesion on SMA showing 28.0% Invasive and 72.0% non invasive*



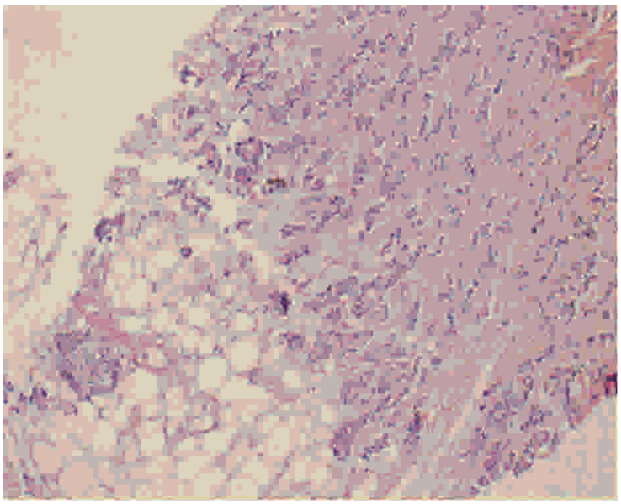
Picture 1: *Tubular Adenoma H&E*



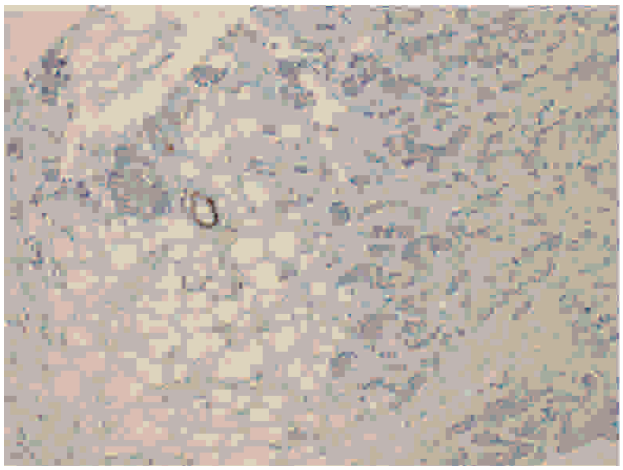
Picture 2: *Tubular Adenoma SMMHC POSITIVE STAINING*



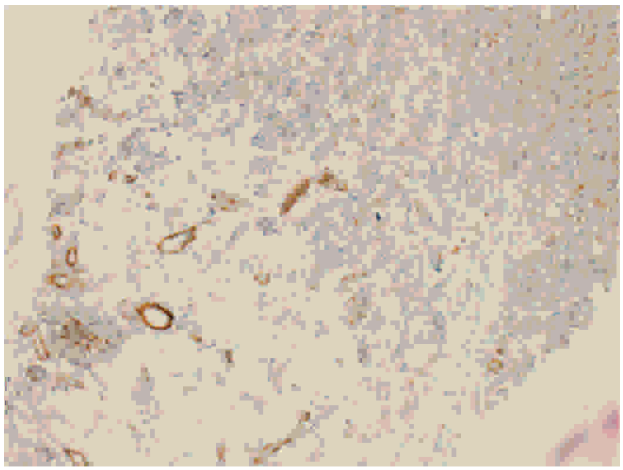
Picture 3: *Tubular Adenoma SMA POSITIVE STAINING*



Picture 4: *Invasive Ductal Carcinoma H&E*



Picture 5: *Invasive Ductal Carcinoma SMMHC NEGATIVE STAINING*



Picture 6: *Invasive Ductal Carcinoma SMMA NEGATIVE STAINING*

DISCUSSION

Carcinoma of the breast is the commonest malignancy in females all over the world and second leading cause of death due to cancer among females. Approximately one in every nine Pakistani women is likely to suffer from breast cancer. This is one of the highest incidence rates in Asia.

Differentiation of benign proliferative breast lesions form malignant tumors is of paramount importance. For this differentiation Trucut core biopsy is frequently carried out to obtain breast tissue for histological examination

The rationale of this study was that in a resource limited setting of our country we need to select the best possible immunomarker for routine diagnostic purposes. This study was undertaken to see the agreement between SMMHC and SMA for differentiation of benign from malignant breast lesions and carcinoma in-situ from microinvasive carcinomas in tru-cut biopsies based on the presence or absence of myoepithelial cell layer. No such study is available from our country so far.

Our study demonstrated an almost perfect agreement between SMMHC and SMA for differentiating non invasive from invasive breast lesion.

In addition our study demonstrated that SMMHC is an easier IHC marker to interpret compared to SMA because it had less cross staining with stromal myofibroblasts. Other studies have also reported cross staining of SMA with stromal myofibroblasts including Lazard D et al 1993[52], Castelluccia L & Milne AW 2003[13], Stefanou D et al 2004[57], Jing HB 2006 [58], Tse GMK et al 2007[60]

No local study has so far compared SMMHC with SMA as MEC markers. These markers have been studied in various international studies. A comparison of this study with international studies is given below in a tabulated form.

The almost perfect agreement between SMMHC and SMA for differentiating non invasive from invasive breast lesion in this study serves our purpose in advocating the use of either SMMHC or SMA in trucut biopsies as an immunomarker for myoepithelial cells.

CONCLUSION

With regards to the agreement between SMS & SMMHC as Myoepithelial cell markers our study reached the following conclusions

1) There is near complete agreement between SMMHC & SMA. Therefore either one of them can be used as a single myoepithelial cell marker in trucut biopsies in our resource limited setting.
2) SMA nevertheless is a slightly more cumbersome stain to interpret subjectively as stromal myofibroblast staining can confound its inter-

Table: *International studies using both SMA &SMMHC*

Year	Authors	SMA antibody	SMMHC antibody	Agreement between stains	Staining performed on	Feature unique to the study
1993	Lazard D et al[52]	SM α actin (Sigma)	SMMS-1	Mostly similar staining for both markers	Frozen tissue sections	Immunofluorescence microscopy used
2003	Castelluccia L & Milne AW[13]	SMA DAKO	SMMHC DAKO	Both markers did not perform the same	Paraffin embedded sections	Antigen retrieval with protease method for SMMHC. SMMHC sections were lifting off glass making staining unclear
2003	Zhang RR et al[55]	α sm-1 Novocastra	SMMS-1 Dako	Mostly similar staining for both markers	Paraffin embedded sections	Modified protocol: incubation of deparaffinized sections at 70°C in the retrieval solution and an incubation for 3–4 hours or overnight of the primary antibody at about 25°C
2009	Hilson JB et al[61]	1A4 Dako (1% reduced expression in DCIS cases)	SMMS-1 Dako (75 % Reduced expression of SMMHC in DCIS cases)	Both markers did not perform the same	Paraffin embedded sections	DCIS cases only
2010	Hilson JB et al[67]	1A4 Dako No reduced expression	SMMS-1 Dako (reduced expression in 21% of MEC of entrapped glands in benign sclerosing lesions)	Both markers did not perform the same	Paraffin embedded sections	Benign sclerosing lesions only
2017	This study	1A4 Dako	SMMS-1 Dako	Mostly similar staining for both markers	Paraffin embedded sections	Staining performed exclusively on trucut biopsy samples

pretation.

3) Routine use of myoepithelial cell marker to differentiate non invasive lesions from invasive lesions is advisable as myoepithelial cells in some cases although present are not identified on H&E.

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HISTOPATHOLOGICAL PATTERN OF ABNORMAL UTERINE BLEEDING IN ENDOMETRIAL CURETTAGE IN FEMALES PRESENTING WITH ABNORMAL UTERINE BLEEDING

Muhammad Akhtar, Sadaf Noor, Ameena Ashraf, Ambereen Anwar, Muhammad Imran, Tazeen Anees

PGRs, Professors, Assistant Professor, Senior Demonstrator, Department of Pathology, Allama Iqbal Medical College Lahore

Abstract

Background: Abnormal uterine bleeding (AUB) is a common presenting complaint in gynecology outpatient department. Patients with AUB have lost cyclic endometrial stimulation that arises from the ovulatory cycle. Dilation and curettage (D&C) are commonly performed for the diagnosis of gynecological conditions leading to AUB.

Objective: To determine the frequency of different types of pathologies in endometrial curettage of females presenting with abnormal uterine bleeding

Material & Methods: Study Design: Cross sectional study. Setting: Department of Pathology, Jinnah hospital, Lahore. Duration: from (9-4-2018) to (9-10-2018). Data collection: 120 patients were enrolled. The specimens were processed routinely and stained with Haematoxylin and Eosin stain. Grossing of specimens done using standard protocols and measurements recorded. Tissue processing performed and slides stained with hematoxylin and eosin stains under strict quality assurance. Microscopic evaluation was done. All the collected data was entered and analyzed on SPSS version 20.

Results: The mean age of patients was 42.13±8.88years. The most common pathologies were endometrial hyperplasia i.e. 47 (39.2%) followed by hormonal imbalance 45(37.5%), endometrium polyp 13(10.8%), endometritis8(6.7%) and endometrial carcinoma 7(5.8%).

Keywords: Endometrial curettage, Abnormal Uterine Bleeding, Females

Abnormal uterine bleeding (AUB) is a common presenting complaint in gynecology outpatient department.[1,2] AUB is one of the most common debilitating menstrual problems and has remained one of the most frequent indications for hysterectomy in developing countries.[3] A systematic clinical approach starting from meticulous history, thorough physical examination, and methodical laboratory investigations will enable the clinician to exclude causes.[4]

Women of childbearing age who are at low risk for endometrial cancer may be assessed initially by transvaginal ultrasonography. Postmenopausal women with AUB should be offered dilatation and curettage.[5] Histopathological evaluation of the endometrial samples plays a significant role in the diagnosis of AUB.[1, 2] Approximately in 40% of hysterectomy specimens, no definite organic pathology could be established.[3] Endometrial curettage is a sensitive and a specific test in and is accurate in diagnosing endometrial pathology. It is found most accurate in diagnosing endometrial pathology.[6]

One study has showed that among females presenting with AUB, endometrial hyperplasia was present in 60.1% and the most common pathology while hormonal imbalance was present in 12.8%, polyp in 10.4%, endometritis in 9.8% and endometrial carcinoma in 6.9% females.[7] Another study has showed that among females with AUB, endometrial hyperplasia was present in 5% only, atrophic endometrium in 6%, polyp was found in 14%, endometritis in 12%, and endometrial carcinoma in 2% females.[3]

The rationale of this study was to assess the

frequency of different types of pathologies in endometrial curettage of females presenting with AUB. It has been observed through literature that hyperplasia is most common pathology of AUB but another study showed to be the least. Both these studies were conducted in Pakistani females. So to confirm the evidence we want to conduct this study. Through this study we will be able to find the most common pathologies in females presenting with AUB from local population. So we conducted this study to find the extent of most common pathology in local population. This would help us in future to plan better management options for better surveillance of patients.

OBJECTIVE

To determine the frequency of different types of pathologies in endometrial curettage of females presenting with abnormal uterine bleeding

METHODS

It is a cross sectional study performed at the Department of Pathology, Jinnah hospital, Lahore. The duration of study is six months i.e. 9-4-2018 to 9-10-2018. A sample size of 120 cases was calculated with 95% confidence level, 5% margin of error and taking expected percentage of hormonal imabalce i.e. 12.8% in females presenting with AUB.[7] It is a non-probability, consecutive sampling with following criteria.

Inclusion criteria: Patients of age 16-68 years presenting with AUB (defined as (a) Post-menopausal bleeding: Any amount of bleeding after cessation of menstruation for >1 year, (b) heavy bleeding >80 ml in a cycle measured by difference between dry and soaked peds considering 1 gm=1 ml, (c) menstrual cycles longer than 38 days as shorter than 24 days or (d) Inter menstrual bleeding) underwent dilatation and curettage and samples will be referred from obstetrics and gynecology department. Exclusion criteria: Patients with recurrent disease (on medical record), low platelet count (<150×10^3/microliter), PT>20 sec, aPTT>15sec

Data collection procedure: D&C samples of 120 patients fulfilling selection criteria were enrolled in study referred to Department of Histopathology, Jinnah hospital, Lahore. Demographic information (name, age, duration of AUB) was also obtained. Then samples were fixed in 10% buffered formalin. The specimens were processed routinely and stained with Haematoxylin and Eosin (H&E) stain. Grossing of specimens done using standard protocols and measurements were recorded. Tissue processing performed and slides were stained with hematoxylin and eosin stains under strict quality assurance. All this information was collected through a predesigned proforma.

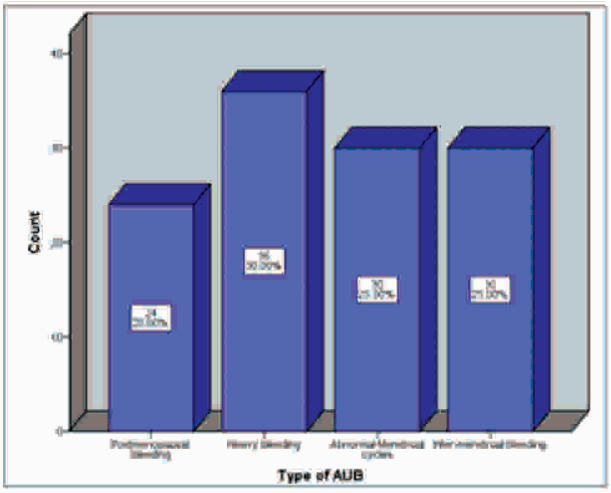
Data analysis: Data was analyzed by SPSS version 20. Quantitative variables like age and duration of AUB was calculated as mean and standard deviation. Qualitative variables like type of AUB and type of pathology i.e. endometrial hyperplasia, ,hormonal imbalance, endometrial polyp, endometritis or endometrial carcinoma was presented as frequency and percentage.

RESULTS

The mean age of the patients was 42.13±8.88 years. The mean duration of symptoms was 3.68±

Table 1: Demographic Characteristics Of Patients

n	120
Age (years)	42.13±8.88
Duration (years)	3.68±1.87

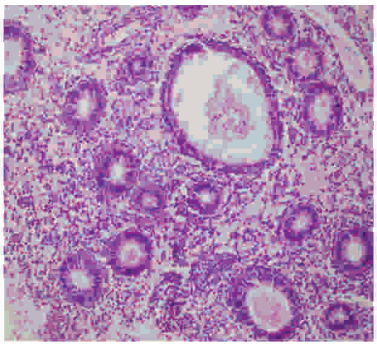


1.87 years. Table 1

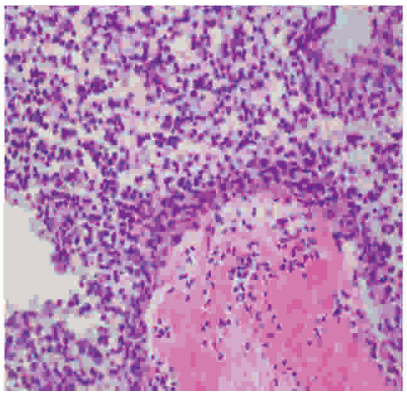
Fig 1: *Distribution of Type of AUB*

There were 24 (20%) patients having post-menopausal bleeding, 36 (30%) had heavy bleeding, 30 (25%) had abnormal menstrual cycle while 30 (25%) had inter-menstrual bleeding. Fig 1

In this study the most common diagnosis was endometrial hyperplasia i.e. 47 (39.2%) followed by hormonal imbalance 45(37.5%), endometrial polyp 13(10.8%), endometritis 8 (6.7%) and endometrial carcinoma 7 (5.8%).



Different morphological patterns seen under



microscope:

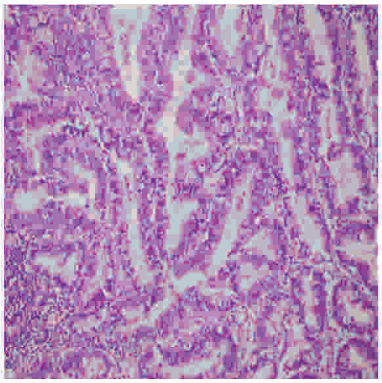


Fig 2: *Histopathology of Hormonal Imbalance 20x*

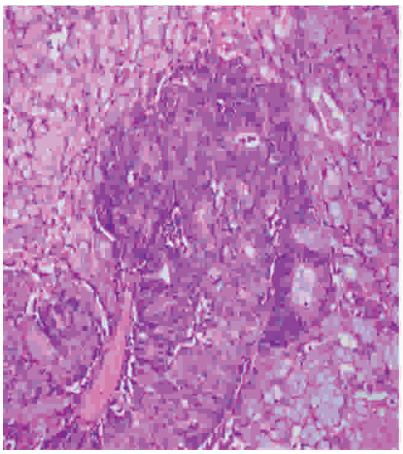


Fig 3: *Histopathology of Endomteritis 20x*

Fig 4: *Histopathology of Endometrial Hyperplasia 20x*

Fig 5: *Histopathology of Endometrial Carcinoma 40x*

DISCUSSION

AUB is one of the most frequently encountered and perplexing condition in adult women. Its causes include a wide spectrum of diseases that may be subdivided into reproductive tract diseases, iatrogenic causes and systemic diseases. Chronic unopposed estrogenic stimulation of the endometrial lining, which is an important cause of AUB, increases the risk of both endometrial hyperplasia and endometrial carcinoma. Many women with AUB may undergo unwarranted hysterectomy without a definite diagnosis.[5,8,9]

AUB is a common diagnosis, making up 5-10% of cases in the outpatient clinic setting.[10] Because most cases are associated with anovulatory menstrual cycles, adolescents[11] and perimenopausal women[12] are particularly vulnerable. About 20% of affected individuals are in the adolescent age group, and 50% of affected individuals are aged 40-50 years. In a study of 400 perimenopausal women, the most common type of bleeding pattern was menorrhagia (67.5%), and the most common pathology was simple endometrial hyperplasia without atypia (31%).[12]

D&C is commonly used in developing countries with limited resources as a standard and often the

only mean of assessing AUB which can be diagnostic as well as a therapeutic procedure.[13] In this study the most common diagnosis was endometrial hyperplasia i.e. 47 (39.2%) followed by hormonal imbalance 45(37.5%), endometrium polyp 13(10.8 %), endometritis8 (6.7%) and endometrial carcinoma 7 (5.8%).

Ayesha Sarwar and Anwar ul Haque conducted a study on type and frequencies of pathologies in endometrial curettings of AUB. They showed in their study that most common complaint was polymennorhagia 36% (18/50) followed by mennorhagia 30% (15/50). There were two cases of oligomennorhoea (2%) and five cases of post-menopausal bleeding (10%). Frequencies of endometrial pathologies wereestrogen dominanance pattern 42% (21), Anovulatory endometrium and chronic endometritis 24%(12) each, atrophic endometrium and endometrial carcinoma 2% (1) each and 6% (3) cases of pill effect endometrium.[14]

One study has showed that among females presenting with AUB, endometrial hyperplasia was present in 60.1% and the most common pathology while atrophic endometrium was present in 12.8%, polyp in 10.4%, endometritis in 9.8% and endometrial carcinoma in 6.9% females.[7] Another study has showed that among females with AUB, endometrial hyperplasia was present in 5% only, atrophic endometrium in 6%, polyp was found in 14%, endometritis in 12%, and endometrial carcinoma in 2% females. Naheed Moghal[15] concluded that histopathological examination of endometrium obtained by curettage remains a valuable approach to an etiological diagnosis particularly in patients with post-menopausal bleeding and metrorrhagia. The diagnostic benefit is low in cases of menorrhagia and intermenstrual bleeding.

Thukkaram Chitra et al.,[16] documented that the commonest histopathological finding was proliferative endometrium (23%) followed by simple hyperplasia (16.2%), secretory endometrium (14.9%) and complex hyperplasia (10.8%). Endometrial carcinoma was diagnosed in 2 patients (2.7%). One study demonstrated in their results that main presenting complaint among our patients was menorrhagia (42.7%). Dysfunctional causes accounted for majority of the cases (61.3%), in which proliferative endometrium was the commonest seen in 159 cases. Organic causes of AUB constitutes (38.7%), the commonest histopathological finding in this category was endometrial hyperplasia which was found in (60.1%) of cases.[13]

Histopathological examination of the endometrial biopsies and curettings revealed various patterns ranging from physiological to pathological lesions of the endometrium. A study by Vaidya et al[17] revealed that proliferative and secretory endometriums were the two most common histopathological patterns which were seen in all the three age groups. Similar observation was made in a study by Abdullah et al.[18] Together, both these patterns were seen in 165 (40.94%) cases. Data from similar studies vary from 28.36% to 53.91%.[19-22]

CONCLUSION

This study concluded that the most common pathologies in endometrial curettage of females presenting with AUB was endometrial hyperplasia, hormonal imbalance, endometrial polyp, endometritis and endometrial carcinomas.

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FREQUENCY OF DEPRESSION AND ITS CONTRIBUTING FACTORS IN PATIENTS WITH POLYCYSTIC OVARIAN DISEASE

Fatima Bukharie, Mariam Iftikhar, Aneel Shafi, Irum Umair, Aafia Malik, Naveed Shahzad Ahmad

Abstract

INTRODUCTION: The syndrome of polycystic ovaries involves hormonal imbalance, mentrual abnormalities, abnormal facial hair growth, acne and polycystic ovaries. It is a fairly common disorder in women of reproductive age. Apart from adverse consequences to fertility and appearance, pco has been associated with adverse mental health outcomes such as depression.

OBJECTIVES:

1. To measure the frequency of depression in patients having PCOS
2. To measure the frequency of factors contributing to depression in patients with PCOS .

STUDY DESIGN: This is a cross sectional study.

SETTING: Gynaecology department sir Ganga Raam Hospital Lahore

DURATION OF STUDY: 6 months (7/5/15---7/11/15)

SUBJECT AND METHODS: 200 patients coming in OPD of Gynaecology of Sir Ganga Ram Hospital Lahore were chosen. (annexure 1) and interviewed after obtaining informed consent. All data was entered into the predesign Performa (annexure 2 attached)in order to get an idea about contributing factors such as hirsutism and bmi (Using the annexures attached)

RESULTS: The results of the study revealed that out of 200 patients 12.5% had depression. The contributing factors were significantly associated with depression. Out of total patients, 5% suffered from mild depression,5% from moderate depression and 2.5% from severe depression. After stratifying the data, we applied chi square test and p value obtained for overall result was less than 0.05 which signified that the modifiers such as age, socioeconomic status and PCODs duration had an impact on depression.

CONCLUSION: Depression was found in 12.5% of the patients of total 200 patients. The contributing factors were assessed and it was shown that acne, hirsutism and BMI was significantly associated with depression and sociodemographic factors also had an impact

Key words: Polycystic ovarian disease, depression , hirsutism, acne ,body mass index

The syndrome of polycystic ovaries involves increased androgens, oligomenorrhea (or amenorrhea) and polycystic ovaries[1] with a prevalence of around 12%[2].

pcos is a commonly encountered clinical entity in practice. women with pcod have higher odds of suffering from depression[3]. Hirsutism, infertility, acne and increase in body weight are the usual contributing factors in depression in pcod sufferers.[4,5]

The studies in this area are scarce in our country. Purpose of our study to get the important data about depression prevalence and also to study role of contributing factors. In case of higher prevalence, we will be able to establish that this is a high risk group and both public and physician need to be aware of it so that holistic care should be made possible for pcod suffers.

OBJECTIVE

1) To measure the frequency of depression in patients having polycystic ovarian syndrome.
2) To study the factors contributing to depression in patients with polycystic ovarian syndrome.

5) OPERATIONAL DEFINITION

5.1. POLYCYSTIC OVARIAN SYNDROME:

PCOS to be present if any 2 out of 3 criteria are

met:

1. Oligo menorrhea (oligomenorrhea was defined as greater than 35 days cycles) or amenorrhea (amenorrhea was defined as less than 3 periods in last six months)
2. Excessive body hair (assessed by Ferriman-gallway method)
3. Polycystic ovaries (by gynaecologic ultrasound showing 12 or more follicles measuring 2-9mm)..

5.2. DEPRESSION:

Depression is a mood disorder in which there is prevailing low mood, lack of pleasure, decreased or lost interest in daily life activities accompanied by thoughts of guilt, pessimism and worthlessness. The mood disturbance should be at least 2 weeks long and be present for most of day in these days. Depression shall be diagnosed according to HAD criteria for depression. cut off point for depression is 8/21. the range for depression is mild (8-10), moderate (11-14) severe (15-21)

5.3.CONTRIBUTING FACTORS OF DEPRESSION IN PCOS:

1) HIRSUTISM: In our study, hirsutism will be evaluated by Ferriman-gallway method (FM). A score above 8 will be labelled as hirsutism. Minimum is 0 and maximum is 36 .

2) INCREASED BODY WEIGHT: It will be estimated by calculating BMI and if the score is equal to or above 30 kg/m^2, it will be labelled as obesity.

3) Acne: Acne will be assessed by Acne Global Severity Scale .score more than or equal to 2 will be labelled as acne(attached as annexure).

METHOD

6.1. STUDY DESIGN:

Cross sectional study.

6.2. SETTING:

We shall conduct our study at psychiatry opd of sir ganga ram hospital Lahore in liaison with gynecology opd of same hospital

6.4. SAMPLE SIZE:

We calculated sample size of 200, taking into account of five percent margin of error and ninety five percent confidence interval, and taking expected percentage of depression that is 12 percent amongst patients having polycystic ovarian disease.

6.5. SAMPLING TECHNIQUE:

Non-probability consecutive sampling technique.

6.6. SAMPLE SELECTION:

Inclusion criteria

- Female patients within the age of 16-45 years.
- PCOS was considered to be present if any 2 out of 3 criteria are met:

1. Oligomenorrhea (cycle longer than thirty five days)or amenorrhea (woman had less than three cycles in last six months)
2. Excessive body hair
3. Polycystic ovaries (by gynecologic ultrasound)

Exclusion criteria

- Females taking oral contraceptive pills.
- Females having any other gynaecological illness, e.g PID and tubal blockage etc.

DATA COLLECTION PROCEDURE

200 patients coming in OPD of Gynaecology of Sir Ganga Ram Hospital Lahore were taken. We first took informed consent, then interviewed each patient individually. All data was entered into the predesign Performa (annexure 2 attached) to determine the contributing factors in the form of hirsutism and body weight. Then Urdu version of HAD symptom checklist (annexure 3 attached) was used to measure the frequency and severity of depression. Contributory factors such as hirsutism was assessed by Ferriman-gallway method (annexure 5) and body weight was assessed by BMI score (annexure 6) and Acne was assessed by Acne Global Severity Scale.

DATA ANALYSIS PROCEDURE

We used SPSS version 12.0 for data entry and analysis. Quantitative data (age, BMI scores) is

presented by deviation (mean and standard deviation). Qualitative data (depression, obesity hirsutism and acne) are presented by frequency and percentages. We stratified our data for age, duration of PCOS, Socioeconomic status to deal with effect malifiers. After data stratification we applied chi square test. We considered a p value of 0.05 or less than that as significant.

RESULTS

A total of 200 female patients coming in the gynecological outdoor with a diagnosis of polycystic ovarian disease were booked for the study. The mean age of females was 30.98 years.

The patients belonged to different socioeconomic background. Around 32% were of lower socioeconomic status, 49.5% hailed from middle socioeconomic status and 18.5% were of high socioeconomic status. Patients up till 6 months after being diagnosed as having polycystic ovarian disease were assessed. It was found that about 5% of the females had mild depression, 5% had moderate depression and 2.5% had severe depression. The contributing factors assessed were acne, hirsutism and Basal metabolic index. It was shown that out of 200 patients 8.5% had mild acne, 4% had moderate acne, 6% had severe acne and 6.5% had severe acne.we applied chi square test to see the correlation between depression and acne and the p value obtained was 0.000, which revealed significant association between the two. BMI was assessed and it was found that 4.5% of the patients were marginally overweight, 8% were overweight and 7% patients were obese. The relation of depression and BMI was assessed and chi square test revealed a p value of 0.000 which signifies the association of depression with BMI. The last contributing factor assessed was hirsutism. It was shown that 13% of the patients had mild hirsutism, 8% had moderate hirsutism and 6% had severe hirsutism. Depression was assessed in terms of hirsutism and chi square test gave a p value of 0.000, which shows that depression is significantly associated with hirsutism. After stratifying the data, chi square test was applied and p value obtained for overall result was less than 0.05 which signified that the modifiers such as age, socioeconomic status and PCODs duration had an impact on depression.

Table Showing Mean And Standard Deviation For Age

Statistics		
AGE		
N	Valid	200
	Missing	0
Mean		30.9800
Std. Deviation		8.20464

Table Showing The Freuency Of Age Group In Study

Statistics		
AGE		
N	Valid	200
	Missing	0

Age					
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Young age	84	42.0	42.0	42.0
	Early middle age	88	44.0	44.0	86.0
	late middle age	28	14.0	14.0	100.0
	Total	200	100.0	100.0	

Table Showing the Socioeconomic Status of The Patient

Statistics		
Socioeconomic Status		
N	Valid	300
	Missing	0

Socioeconomic Status					
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	low socioeconomic status	64	32.0	32.0	32.0
	middle socioeconomic status	99	49.5	49.5	81.5
	high socioeconomic status	37	18.5	18.5	100.0
	Total	200	100.0	100.0	

***Table** Showing The Duration of Pcos*

Statistics		
PCOs Duration		
N	Valid	200
	Missing	0

PCOs Duration					
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	1 month	22	11.0	11.0	11.0
	2 months	29	14.5	14.5	25.5
	3 months	28	14.0	14.0	39.5
	4 months	40	20.0	20.0	59.5
	5 months	34	17.0	17.0	76.5
	6 months	47	23.5	23.5	100.0
	Total	200	100.0	100.0	

***Table** Showing the Frequency of Depression in Patients with Pcods*

Statistics		
HADs		
N	Valid	200
	Missing	0

HADs					
		Fre-quency	Percent	Valid Percent	Cumulative Percent
Valid	Normal	175	87.5	87.5	87.5
	mild depression	10	5.0	5.0	92.5
	moderate depression	10	5.0	5.0	97.5
	severe depression	5	2.5	2.5	100.0
	Total	200	100.0	100.0	

***Table** Showing Frequency of Depression and Hirsutism and their Relationship*

Case Processing Summary						
	Cases					
	Valid		Missing		Total	
	N	Percent	N	Percent	N	Percent
HADs * Hirsutism	200	100.0%	0	.0%	200	100.0%

HADs * Hirsutism Cross-tabulation						
% of Total						
		Hirsutism				
		no hirsu-tism	mild hirsu-tism	moderate hirsutism	severe hirsu-tism	Total
HADs	Normal	73.0%	9.5%	3.5%	1.5%	87.5%
	mild depression		.5%	3.5%	1.0%	5.0%
	moderate depression		2.0%	.5%	2.5%	5.0%
	severe depression		1.0%	.5%	1.0%	2.5%
Total		73.0%	13.0%	8.0%	6.0%	100.0%

***Table** Showing Chi Square Test Applied to See the Association of Depression and Hirsutism*

Chi-Square Tests			
	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	132.980[a]	9	.000
Likelihood Ratio	94.141	9	.000
Linear-by-Linear Association	78.689	1	.000
N of Valid Cases	200		

a. 10 cells (62.5%) have expected count less than 5. The minimum expected count is .30.

***Table** Showing the Frequency of Depression and the Body Mass Index of Patients*

Case Processing Summary						
	Cases					
	Valid		Missing		Total	
	N	Percent	N	Percent	N	Percent
HADs * BMI	200	100.0%	0	.0%	200	100.0%

HADs * BMI Crosstabulation						
% of Total						
		BMI				
		normal	marginally overweight	Over-weight	obese	Total
HADs	normal	79.0%	3.0%	1.5%	4.0%	87.5%
	mild depression		.5%	3.0%	1.5%	5.0%
	moderate depression	1.5%		2.5%	1.0%	5.0%
	severe depression		1.0%	1.0%	.5%	2.5%
Total		80.5%	4.5%	8.0%	7.0%	100.0%

***Table** Showing Chi Square Test Applied to See the Association of Depression and Body Mass Index (bmi)*

Chi-Square Tests			
	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	116.442[a]	9	.000
Likelihood Ratio	85.316	9	.000
Linear-by-Linear Association	55.346	1	.000
N of Valid Cases	200		

a. 10 cells (62.5%) have expected count less than 5. The minimum expected count is .23.

Table Showing the Frequency of Depression and Acne of Patients

Case Processing Summary						
	Cases					
	Valid		Missing		Total	
	N	Percent	N	Percent	N	Percent
HADs * Acne	200	100.0%	0	.0%	200	100.0%

HADs * Acne Crosstabulation								
% of Total								
		Acne						
		clear	almost clear	mild acne	moderate acne	severe acne	very severe acne	Total
HADs	Normal	23.0%	52.0%	6.0%	2.0%	2.5%	2.0%	87.5%
	mild depression			.5%	.5%	2.0%	2.0%	5.0%
	moderate depression			1.0%	1.0%	1.5%	1.5%	5.0%
	severe depression			1.0%	.5%		1.0%	2.5%
Total		23.0%	52.0%	8.5%	4.0%	6.0%	6.5%	100.0%

Table Showing Chi Square Test Applied to See the Association of Depression and Acne

Chi-Square Tests			
	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	112.413[a]	15	.000
Likelihood Ratio	91.895	15	.000
Linear-by-Linear Association	66.394	1	.000
N of Valid Cases	200		
a. 16 cells (66.7%) have expected count less than 5. The minimum expected count is .20.			

DISCUSSION

Previous researches have highlighted the role of psychiatric comorbidity in pcod.cooney et found that women with pcod have 3-4 times the odds ratio for normal population for suffering from anxiety and depressive symptoms. When we look at cardinal features of pcod, it is not difficult to understand their possible role in contributing to stigma, low self esteem, hopelessness and social pressures that these sufferers have to undergo. studies have highlighted that pcod affects all domains of functioning in a woman's life, including sleep disturbances[7] and sexual dysfunction[8]. In the current study, patients were assessed for depression and it was found that 12.5% of the female patients suffering from PCODs had depression. Previous literature also revealed that depression in PCODs were present in around 12-14% of the patients[9,10]. Some studies however have found a much higher prevalence of depression in pcod eg ozdimer o et al[11] found that 49.3% of women with pcod were depressed. On the other hand some studies have reported a prevalence rate lower than our study eg green wood et al[12] found 8.4% prevalence of depression in pcod. These differences can be explained in terms of differences in characteristics of study populations. Our study also found an important contribution of hirsutism, BMI ,acne to depression. various other studies have found role of these factors in depression in pcod as well as their adverse effects on quality of life[13,14]. still other study found other factors like menstural problems[15] sleep disturbances[7] hormonal imbalances[16] and role of impaired CRH[17] in causing depression in pcod. A study by Khomami et al18found hirsutism to be strongest contributing factor.

The present study also assessed the sociodemographic factors such as age, duration of PCODs and socioeconomic status as parameters that may have an impact on the results and found that these factors do effect results and contribute to depression. The previous studies didn't find any association between depression and sociodemographic factors.

CONCLUSION

A total of 200 females patients coming to the

gynecological outdoor with a diagnosis of PCODs were assessed for depression. Depression was found in 12.5% of the patients. The contributing factors were assessed and it was shown that acne, hirsutism and BMI was significantly associated with depression. Moreover, it was seen that the sociodemographic factors such as age, socioeconomic status and duration of PCODs also had an impact on overall result and thus enhancing the effect of contributing factors.

LIMITATIONS OF THE STUDY

Despite our most sincere efforts some limitations of our study have to be considered. First it was a single center based study and secondly being a descriptive study, its place in evidence based medicine is inferior to Randomized controlled trials.

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FREQUENCY OF DEPRESSION IN FAMILY CAREGIVERS OF CANCER PATIENTS UNDER TREATMENT

Aneel Shafi, Aafia Malik, Ayaz M Khan, Aayesha Riaz , Fatima Bukharie, Nouman Ahmad

Abstract

Introduction: Care givers can be divided into two categories, formal(professional) care givers and informal caregivers that are usually family members. The later variety of care giving is expected to have high levels of chronic stress. This would negativly effect their quality of life

Objective: To find the frequency of depression among family caregivers of cancer patients under treatment in a tertiary care hospital

Material & Methods: Study Design: Cross sectional study. Setting: Department of Psychiatry, Jinnah Hospital, Lahore. Duration: 6 months(3/12/2016----3/6/2017)Data Collection: Total230 patients were enrolled and Hospital Anxiety and Depression Scale (HADS) was used to have a discussion with caregiver of cancer patients. If the score of caregiver was ≥11, then depression was labeled.

Results: Mean age of caregiver in this study was 38.77±12.56 years. There were 110(47.83%) male and 120(52.17%) female caregivers in this study. Mean duration of care given by the care givers was 1.97±0.82 years. Mean HADS score was 8.45±4.70. As per operational definition depression was diagnosed in 79(34.35%) care givers. NO statistically significant association was seen between care givers, age, gender and care giving duration.

Conclusion: Not only patients with cancer develop depression but their care givers at the same time have the tendency to develop depression. So it is important that clinicians should guide and plan some management or surveillance campaigns which may decrease depression among caregivers and they will take care of their cancer patient in a better way as well.

Key Words: Depression, Family, Caregivers, Cancer patients, Treatment, Tertiary care hospital

Since cancer is major illnesses so if some one is diagnosed with it, both the patient and his family can be expected to face great stress studies show that the stress in partner and off spring of cancer patient are similar to that of patient and this hints at common factors causing distress in such families.[1]

Most families of cancer patient experience heightened stress due to various reasons. They may be preoccupied with thoughts of suffering and pain that their loved one has to bear. They may be worried about prospects that they may lose their loved ones. Also care giving means a lot of work burden on them and they may be angry as now they have to do more at home.[2]

Grief which is a normal psysiological response to any significant personal loss can be evident in the lives of both terminally ill patient and his family but it usually decreases as time passes.[3]

One study done in Korea found that depression was present in 35% caregivers of cancer patients' caregivers reflecting high prevalence in them.[4] Another study conducted in Canada also observed that 30% of family caregivers develop depression.[5] Segrin et al. (USA) found depression was 33% of relatives of cancer patients.[6]

But a study conducted Turkey found that the depression was present in 17.6% family caregivers.[7] Gozum et al., (Turkey) also supported the evidence and reported that only 11.8% of relatives of cancer patients were reported to be depressive.[8]

Rationale of my study is to assess the frequency of depression among family caregivers of cancer patients under treatment in a tertiary care hospital. In routine, it is noticed that cancer patient has some sort of depression and fear of losing life and mostly

physicias focus on management of rehabilitation of psychological feature of cancer patient. But the relatives, particularly caregivers of cancer patient may also develop depression but usually it is not considered as important. It is also noticed that there is no local evidence present regarding the incidence of depression among family caregivers of cancer patients. This will help us to attain local data moreover, it will help to plan some management or surveillance campaigns which may decrease depression among caregivers and they will take care of their cancer patient in a better way as well.

OBJECTIVE

To find the frequency of depression among family caregivers of cancer patients under treatment in a tertiary care hospital

MATERIALS AND METHODS

Study Design: Cross sectional study

Setting: Department of Psychiatry, Jinnah Hospital, Lahore

Duration of Study: Six month(3-12-16----3-6-17)

Sample Size: Sample size of 230cases was calculated with 95% confidence interval, 5% margin of error and taking expected percentage of depression i.e. 17.6% in family caregivers of cancer patients under treatment in a tertiary care hospital.

Sample Technique: Non-Probability, consecutive sampling

Sample Selection

Inclusion Criteria: Persons (male and females) of age 20-60 years of either gender presenting with cancer patients (all types of cancers included) as family caregivers (spouse, siblings, parents or children of cancer patients living with or taking care of cancer patient) providing care for at least 6 months.

Exclusion Criteria: Relatives of cancer patient presenting in hospital first time with them or not providing them family care

Data Collection Procedure: Total 230 patients fulfilled the selection criteria were enrolled in the study. Informed consent was taken. Demographic data was also be noted. Then Hospital Anxiety and Depression Scale (HADS) was used to have a discussion with caregiver of cancer patients. If the score of caregiver was ≥11, then depression was labeled (if HADS score of caregiver of cancer patient ≥11). Odd number questions from 1-14 was asked). All this information was recorded in a proforma. All persons diagnosed with depression in this way were offered comprehensive treatment (pharmacological and psychological) through psychiatry OPD.

Data Analysis: Data was entered and analyzed by SPSS version 20. Quantitative variables like age was presented as mean and standard deviation. Qualitative variables gender, and depression was presented as frequency and percentage. Data was stratified for age and gender of caregiver and duration of care giving. Post stratification, chi-square test was applied taking p-value≤0.05 as significant.

RESULTS

Mean age of caregiver in this study was 38.77± 12.56 years. There were 110(47.83%) male and 120(52.17%) female caregivers. Mean duration of care given by the care givers was 1.97±0.82 years. Mean HADS score was 8.45±4.70. Table 1

Depression was diagnosed in 79(34.35%) care givers. Fig 1

Among the diagnosed depression care givers 30(38%) were in the age group 20-30 years followed by 13(16.5%) in 31-40 years, 11(13.9%) in the age group 41-50 years and 25(31.6%) in the age group 51-60 years. It was observed that most of the care givers in younger and older age group suffered from depression more. But statistically no significant association was seen between age group of care givers and frequency of depression. i.e. (p-value= 0.152). Care givers who were diagnosed with depression among t hem 39(49.4%) were male and 40(50.6%) were females. No statistically significant association was seen between gender of the care givers and depression. i.e. (p-value=0.735). Caregi-

vers in which depression was diagnosed among them 32(40.5%) were giving care for the last 1 years, 20(25.3%) were giving care for the last 2 years and 27(34.2%) were giving care for the last 3 years. As per this trend no statistically significant association was seen between duration of caregiving and depression faced by the care givers. i.e. (p-value= 0.216).Table 2

Table 1: *Characteristics of Patients*

n	230
Age (years)	38.77±12.56
Male: female	110 (47.8%) : 120 (52.2%)
Duration Of Care	1.97±0.82
HADS score	8.45±4.70

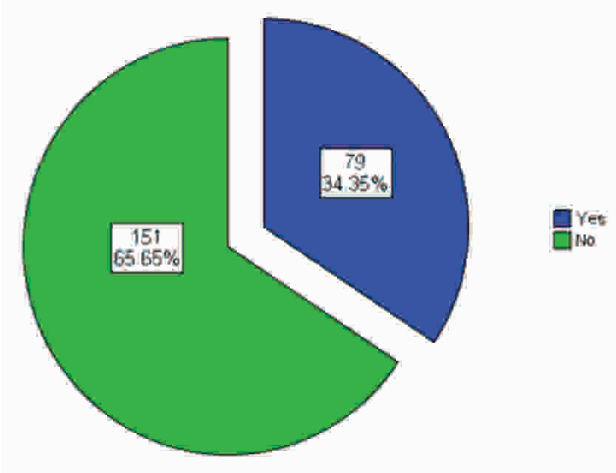

FIGURE-1: *depression*

Table 2: *Comparison of Depression in Strata*

	Depression		***Total***	***p-value***
	Yes	***No***		
Age Groups				
20-30	30(38.0%)	48(31.8%)	***78***	***0.152***
31-40	13(16.5%)	50(21.7%)	***50***	
41-50	11(13.9%)	43(18.7%)	***43***	
51-60	25(31.6%)	59(25.7%)	***59***	
Gender				
Male	39(49.4%)	71(47%)	**110**	***0.735***
Female	40(50.6%)	80(53%)	**120**	
Duration of Care giving				
1 year	32(40.5%)	49(32.5%)	***81***	***0.216***
2 years	20(25.3%)	55(36.4%)	***75***	
3 years	27(34.2%)	47(31.1%)	***74***	

DISCUSSION

Family members often provide caregiving in various ailments and conditions. Such informal caregivers often face considerable stress that may negatively effect their lives and health.[9]

There are several studies that have shown that family care givers of sufferers with cancer face heightened stress that effect their lives.[10-12] This psychological tension even increases when the caregivers have little emotional and practical support and limited time available to rest and to take care of oneself.[13] Symptoms of depression significantly affect care givers' lives and their prevalence varies from twelve to thirty percent.[13, 14] Demography of patient and caregiver play important role in determining depressive symptoms.

Tasks of care and increased burden of care increases the depressive symptoms but positive beliefs and positive appraisal of stressful circumstances decrease stress and depressive symptoms as elaborated by Lazarus and Folkman in their stress coping model.[10, 15, 16] Antonovsky found that a strong sense of coherence in care giver can foster a resilience in them to withstand increased stress and to avert psychological sequelue to them in caring for cancer patients.[17]

Results of current study showed that mean HADS score of caregivers was 8.45±4.70 and 79(34.35 %) caregivers suffered from depression. Peak of depression was seen in the younger and the older caregivers i.e. 20-30 (38%) years and 51-60 (31.6%) years. Frequency of depression was almost same in male and female caregivers i.e. Male: 49.4% & Female:50.6%. Duration of care giving was not associated with depression among caregivers.i.e. 1 Year: 40.5%, 2 years: 25.3% and 3 years: 34.2%.

Boyoung Park in his study stated that depression symptoms had a prevalence of 82.2% in cancer patients' family care givers18.Another study which was done in Korea, stated that depression had prevalence of sixty seven percent in family caregivers of cancer patients.[19] In our study frequency of depression was quite low when compared with the

frequency reported by Boyoung Park and in Korean study.

According to Hislilimitpoint, 35.2% cancer patients had depression while about of their family caregivers had depression..[20] Segrin et al reported that thirty two percent patients with breast cancer and thirty three percent of their family relatives were depressed.[6]

Frequency of depression among care givers of this study is almost same to that of reported by Segrin but higher than the frequency of depression reported by Hislilimit.

A Turkish study done by Gozum et al found that among cancer patients, 53.2%were depressed while 11.8% of their family relatives were depressed.[8] Frequency of depression reported by Gozum was also a bit higher than that of this study. One major reason of difference in prevalence of depression in ours and other studies can be that composition and characteristics of our population might be different than them.

The study by Xiaoshi Yang reports a very high prevalence(67.8%) of depressive symptoms in family caregivers of cancer patients of Chinese origin. This is much higher than that in non Chinese population.[5,21]

This difference in frequency of depression among care givers may be due to sample size difference or some methodological differences for measurement of depression among caregivers. But the main difference can be explained on the basis of cultural/ethnic values difference. In our set up the treatment of cancer patients is very much expensive but at Government level some tertiary level hospitals providing the treatment to cancer patients free of cost but still caregivers had a strong emotional relation and affiliation especially in this part of the world may be a protective factor for caregivers. We don't have specialized palliative care centers for such patients. However economical problems, lack of members for care giving and other social, psychosocial and interpersonal characteristics makes it a bit difficult for the caregivers not to stay stress free.

Caregivers' demographic details had a strong association with depression. Also low monthly income of caregivers and less sleeping hours were positively associated with depression.[22,23]

Since stress is almost unavoidable in caring for a seriously ill loved on, it is important that we should be able to predict which caregiver is at higher risk for depression. It is possible if we keep in mind the high risk associated factors with depression in caregivers. One limiting factor in identifying such patients is the limited access to primary care physicians. [9]

Researches have also showed that providing proper informational care to cancer patients and their caregivers can help in reducing levels of depression in them. So it is important to work in this area too. Also cancer treatment is a complex multistage treatment which also requires that adequate psychosocial support be provided to cancer patients and their caregivers in various different stages of illness and its treatment on an individualized basis.

CONCLUSION

Results of this study suggest that not only patients with cancer develop depression but their care givers at the same time have the tendency to develop depression. So it is important that clinicians should guide and plan some management or surveillance campaigns which may decrease depression among caregivers and they will take care of their cancer patient in a better way as well. So it is essential that we include proper assessment as well as psychosocial support to caregivers as a part of a comprehensive care package.

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EFFECTIVENESS OF HEALTH EDUCATIONAL PROGRAMME ON KNOWLEDGE REGARDING PREVENTION OF WORM INFESTATION AMONG SCHOOL GOING CHILDREN

Zafar Iqbal Bhatti[1], Imran Yasin[2], Khurram Nawaz[3], Khawar Abbas Chaudhary[4], Asif Aleem[5], Mujtaba Hasan Siddiqui[6]

[1]Assistant Professor Department of Pediatrics, Niazi Medical & Dental College, Sargodha, Pakistan; [2]Senior Registrar, Department of Pediatrics, Continental Medical College, Lahore, Pakistan; [3]Assistant Professor, Department of Pediatrics, Shahida Islam Medical & Dental College, Lodhran, Pakistan; [4]Associate Professor, Department of Medicine, Continental Medical College Lahore, Pakistan; [5]Associate Professor, Department of Pediatrics, Continental Medical College Lahore, Pakistan; [6]Assistant Professor, Department of Medicine, Akhtar Saeed Medical and Dental College, Lahore, Pakistan

Abstract

Worm infestation is considered as more prevalent disease in Pakistan silently affecting the children. Worm infestation is more prevalent among school children. It leads to multiple complexities in children, among those nutritional deficiencies and retarded growth is common. Knowledge of the worm infestation can assist in early detection of the diseases and to reduce the incidence of complications. The present study was carried out to investigate the role of teaching services among school children studying at selected schools of Punjab about preventable measures regarding worm infection. A pre-experimental study with one group-pretest and post test design by using simple random sampling was done. 250 school going children were selected. Health educational program was used to establish the pre-test knowledge score and health educational program was administered for selected school going children and post-test was conducted to establish the effectiveness of health educational package on knowledge regarding prevention of worm infestation. It is evident from the result that pre-test knowledge means score was found to be 11.54 as compared to the post test mean score of 16.41. Further, the enhancement of mean score was found to be 4.87. However, the statistical paired t-test indicate the enhancement of knowledge was found to be highly significant ($t= 12.88$, $p< 0.05$) revealing the effectiveness of health educational package on knowledge regarding prevention of worm infestation. It is concluded that health educational program showed the highly significant effect on knowledge regarding prevention of worm infestation.

Keywords: School Going Children, Prevention, Worm Infestation.

The magnitude of parasitic infestations among children constitutes a major health problem in many parts of the world. Six hundred million people worldwide are infected with hook worm and one billion each with round worm and whip worm.[1] Ascariasis is common during preschool period from 1-5 years of age when the child begins to lay a more independent life.[2]

According to WHO, 91% prevalence rate was found globally. In developing countries the problem is considered as among most commons health issues encountered especially among under five children. WHO recommended that prevalence rate need to be reduced by 10% every year to improve the health economics of the developing countries. It is the responsibilities of the health care professional to fulfill the goal of the WHO.[3]

It is estimated that among children, age group

Correspondence: Dr. Zafar Iqbal Bhatti, MRCP, DCH (Ireland), MRCPS, DCH (Glasgow-UK).
Assistant Professor, Department of Pediatrics, Niazi Medical & Dental College Sargodha, Pakistan
Email: drzibhatti@gmail.com

of three months to three years is at more risk for malnutrition which could develop as an early or late manifestation of worm infection. Children can be expected to have intestinal parasitic infection soon after weaning and high risk of re infection in the rest of his/her life. The common reasons related to this etiology are, impure water for drinking purpose, poverty, improper sanitary condition, and parents having low educational level.[4]

Common relevant disorders caused by Worm infection in children are imbalanced nutrition, poor mental and physical growth and blood deficiencies. The most significant effects related to worm infection are respiratory and gastrointestinal disorders prevalent in children.[5] The most persistent respiratory and gastrointestinal disorders cause illness and frequent deaths in children due to worm infections. It is reported that worm infections are responsible for twelve percent of overall child diseases that happen especially in school children having age group of five to fourteen years.[6]

Both primary and secondary malnutrition is the main cause of children mortality and morbidity. Primary malnutrition in children is mainly due to lack of basic food whereas infectious diseases and worm infestation are mainly responsible for secondary malnutrition in developing countries.[7] Micronutrient deficiencies (MND) including iron, zinc, iodine, folic acid and vitamin A also contribute significantly in malnutrition. Among these, preschool children contribute 47.4% with highest burden in Africa and Asia.[8]

Iron deficiency anemia is considered as significant problem associated with hookworm infection. PEM the common disorder of children nowadays is linked with roundworm and whipworm infections.[9] The main problem concerning the issue of worm infection is mental abilities of children like learning and cognitive which are commonly affected. Helminthic infection is considered a serious health issue because the problem is misdiagnosed due to other consequences related to worm infection.[10] The common worm infestation in our community is Ascaris Lumbricoids (round worm), Ankylostoma Duodenale (Hook Worm) EnterobiousVermicularis (Pin Worm) and threads worms and tap worm. In most of these cases, malnourished children continue their poor growth in early school going age which affects their physical and cognitive growth.[11]

Health education is an effective method to provide knowledge, modified the wrong knowledge, belief and practice regarding worm infection. Appropriate knowledge and practice related to worm infection is a key in its management and good health of child. With health education, there lies disease prevention which focus to lower the risk factors for the disease.

The aim of the study is to assess the effectiveness of health education on knowledge regarding prevention and management of worm infection in school age group children in rural community.

Hypothesis:

Null Hypothesis:

Health educational programme is not effective in improving knowledge regarding prevention of worm infestation among school going children

Alternative Hypothesis:

Health educational programme is effective in improving knowledge regarding prevention of worm infestation among school going children

METHODS

SETTING

This study was conducted in Govt. Schoolin Chuhang, MultanRoad, Lahore.

RESEARCH DESIGN

A quasi-experimental study design is used.

POPULATION

The target population of the study was 250 students of 3-5th class in selected school of Chuhang, MultanRoad, Lahore, Lahore.

SAMPLING

Convenient sampling technique was used in this study.

RESEARCH INSTRUMENT

A well-structured and adopted questionnaire used in order to collect the data from the participants.

ANALYZE DATA

Data analysis is done on SPSS (version 21).

- Data related to demographic variables were analysed in percentage and frequency form by using bar charts.
- Paired T-test was used to analyse the pre and post data collection regarding the importance of well-balanced nutrition.

STUDY TIME LINE

This study took 3 years (September 2015, to December 2018).

ETHICAL CONSIDERATION

The rules and regulations were followed while conducting the research and the rights of the research participants were respected.

RESULTS

Out of 250 school going children majority of 129 (51.6%) subjects were from the age group of 11-12 years, 121(48.4%) were in the age group of 8-10 years. 131(52.4) subjects were male and 119(47.6%) were female. Educational status shows that majority of subjects 97 (38.8%) were in 5th standard. Type of family shows that 126 (50.4%) subjects were living in joint family, the number of children in the family were 106 (42.4%), three children. Place of residence shows that183 (73.2%) subjects were living in urban area. According to dietary pattern, 163 (65.2%) subjects were vegetarian. Majority of subjects, 157 (62.8%) were drinking tap water, Majority of 207 (82.8%) subjects were drinking filtered water. Based on method of purification of water, majority of the 154 (61.6%) subject families used boiling as a method of purification of water. Majority 227 (90.8%) subjects were using sanitary latrines. Most of the subjects 198 (79.2%) were not having any previous history of worm infestation. Source of information shows that 143 (57.2%) subjects got information regarding worm infestation through mass media.

This table represents the pretest mean knowledge score was 11.54 and test mean knowledge score was 16.41. Further, the difference means knowledge score on prevention of worm infestation among school going children found to be 4.87%.

The paired t test value 12.88 shows that there was a statistically significant improvement between pre and posttest knowledge score on prevention of worm infestation of the subjects at 0.05 level degree

Table 1: Frequency and Percentage Distribution of the Subjects as per Pretest Knowledge Score

NOWLEDGE LEVEL	RANGING SCORE	SCHOOL GOING CHILDREN	
		F	%
GOOD	< 50% SCORE	139	55.6%
AVERAGE	51-75% SCORE	100	40.0%
POOR	>75% SCORE	011	04.4%

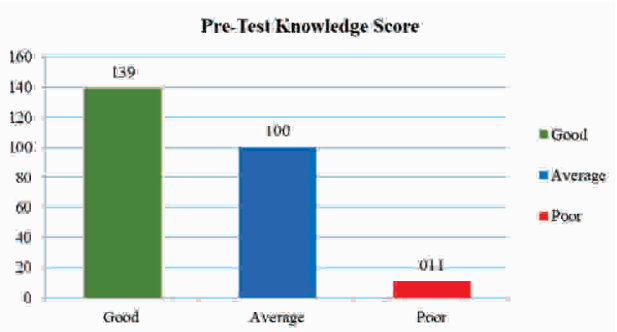


Table 2: Frequency and Percentage Distribution of the Subjects as per Posttest Knowledge Score N=250

NOWLEDGE LEVEL	RANGING SCORE	SCHOOL GOING CHILDREN	
		F	%
GOOD	< 50% SCORE	179	71.6%
AVERAGE	51-75% SCORE	046	18.4%
POOR	>75% SCORE	025	10.0%

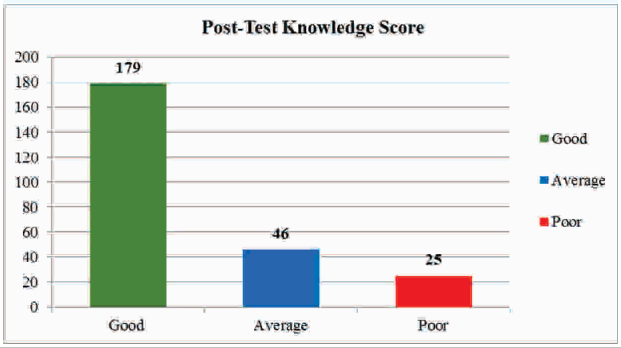


Table 3: *Comparision Between Pre And Post Test Knowledge Scores on Prevention of Worm Infestation Among School Going Children N=250*

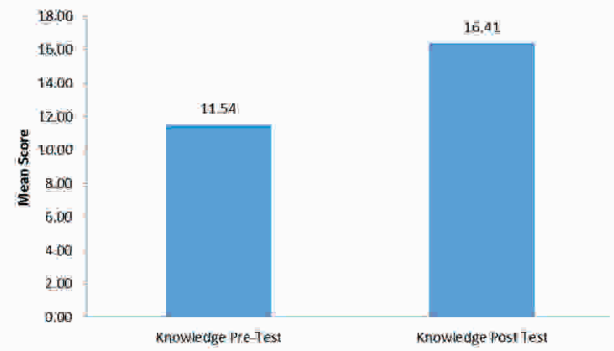
Test	Items	Mean	Std. Deviation	Std. Error Mean	Mean Difference	Paired T-Test	P-Value
Knowledge Pre-Test	250	11.54	3.82	0.24	4.87	12.88	.0001**
Knowledge Post Test	250	16.41	4.65	0.29			

of freedom.

DISCUSSION

Worm infestation is the common and neglected problem among school children especially in rural areas. Keeping this view in mind the present study was undertaken in government school with an objective to assess the effectiveness of health education program on prevention of worm infestation.

The structured teaching programme was found



to effective in increasing the knowledge of school children regarding prevention of worm infestation. The mean gain difference between posttest and pretest knowledge scores was 4.87 which were statistically significant. Similar studies also showed increase in the knowledge scores of school children after implementing structured teaching programme on prevention of worm infestation[12]. One of another study[13] conducted also reported the same results as there was increase in the post test knowledge scores of children after implementing STP and the resulted peak increase in the score was highly significant. There was no significant association between pretest knowledge score with their selected demographic variables at 0.05 level of significance.

Knowledge scores of students were found to have significant association with certain socio demographic variables such as class and mode of defecation[14] whereas one of the other study[15] reported that there was no significant relationship between the posttest knowledge score and selected demographic variables.

CONCLUSION

It is concluded that health educational program showed the highly significant effect on knowledge regarding prevention of worm infestation.

Teaching programme focus should be placed on providing basic services to children so that a healthy nation can be developed. Hence the study concluded that knowledge level among school going children regarding prevention of worm infestation was inadequate before the administration of health educational package. The health educational package was effective in increasing the knowledge of school going children, that is overall and in all knowledge aspects in the post test score were high compared to the pretest score.

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EVOLVING SUSCEPTIBILITY PATTERN OF TYPHOIDAL SALMONELLA

Mariam Danish Iqbal, Farhan Rasheed, Ahmad Yar, Umme Farwa, Kanwal Hassan Cheema, Fatima Hameed

Microbiology Department, Combined Military Hospital, Lahore

Abstract

Background & Objectives: Food-borne Salmonella infections are a worldwide concern. Its isolation is usually increased during the spring/summer season, due to lack of hygiene and increased spoilage of food.1 Sensitivity patterns are changing and evolving all the time. It is useful to be aware of the species which are prevalent in this area to improve the adequate empirical therapy for treating salmonella infections.

Methods: This was a cross sectional study conducted at Microbiology department, CMH, Lahore, from May 2015 to September 2015. Salmonella isolates were identified on the basis of Gram stain, Catalase, Oxidase test, API 20 E and confirmation was done by serology. Antibiotic susceptibility was done by Modified Kirby Bauer method following CLSI 2015 guidelines.

Results: A total of 30 isolates of Salmonella were isolated during 6 months. Quinolones were resistant to 80% of isolates. Ampicillin was resistant to 100% isolates. Surprisingly chloremphenicol was resistant to only 47% of isolates. Co trimoxazole showed resistance to 93% of isolates. Ceftriaxone was susceptible to 100% isolates. Out of the 30 samples 18 are in the paediatric age group , ie ages 5 months- 12 years. The remaining 7 were from adults out of which 2 were from patients older that 50 years.

The male to female ratio was 18: 11. (1.6:1)

The percentage of MDR salmonella, MDR salmonella is that which is resistant to ampicillin, Cotrimoxazole, and Chloremphenicol, is 47%.

Conclusion: The results lead to the conclusion that quinolones are no longer the drug of choice in our setup, but in fact if suspected or confirmed, the drug of choice should be third generation cephalosporins. The awareness of this knowledge is important to prevent the inappropriate use of statistically resistant antibiotics. Prescribing antibiotics which are most likely resistant, may lead to increased morbidity of patient.

Key words: Salmonella, MDR, antibiotics, sensitivity

Salmonella species are a cause of acute enteric fever, which is a big concern in South East Asia, and especially Pakistan. Of the 21.6 million infected patients around the world, 90% morbidity and mortality occur in Asia. It is mainly attributed to poor sanitary hygienic conditions, especially due to contaminated water supplies. The species responsible for causing Enteric fever are Salmonella Typhi, Salmonella Paratyphi, and Salmonella Cholerasuis.[1]

The disease may be acute non complicated (characterized by prolonged fever, disturbances in bowel functions headache, malaise, and anorexia) and complicated which is characterised by intestinal bleeding, melena, intestinal perforation, and peritonitis.

According to the WHO, of the 21.6 million infected individuals infected around the world, 1-5% become carriers.[2] A carrier is defined as a person that harbors and transmits the causative agent systemically, but is asymptomatic or immune to it. Due to hospitalization and and other associated reasons, enteric fever has a very high socioeconomic impact on society and healthcare resources as a whole.

Antimicrobial susceptibility testing is essential for clinical management. This is especially due to multidrug resistance developing over the years.[3]

Correspondence: Dr. Mariam Danish Iqbal, Email: mariamsaeed@ hotmail.com

Chloramphenicol, Ampicillin, and Cotrimoxazole were considered as first line drugs for typhoid fever. Typhoid fever causing salmonella species became resistant to chloremphincol and ampicillin in the 1970's. Cotrimoxazole resistant species starting making their appearance in the late 1980's.[1] Bacteria resistant to all three primary antibiotics were now known as multidrug resistant starins. In the 1990's and onwards this leaves the alternative drugs of flouroquinlones, and cephalosporins.[4]

During the writing of this article, ceftriaxone was the drug of choice for the treatment of acute enteric fever.[5] This study was conducted to detect antimicrobial susceptibility of local salmonella isolates, and evaluate the current trends in sensitivity patterns.

METHODS

The study was a cross sectional one, conducted at Microbiology department, Combined Military Hospital, Lahore. It was a six-month study from May 2015- September 2015. A total of 151 blood samples were processed from febrile patients presenting to the outpatient department.

The blood samples were collected by venipuncture under aseptic conditions. The blood samples were collected by venipuncture under aseptic conditions in BHI broth and then sub cultured on solid medium such as MacConkey and Blood agar, after every 24 hours of incubation and subsequently, according to lab protocol. The recommended volume of blood to broth ratio is 1:5- 1:10.6

The Non lactose fermenting colonies on MacConkey agar were subjected to identification following standard procedures. This included Gram staining, biochemical profile (using API 10S), and serotyping.

Isolates identified as Salmonella species, were then subjected to antibiotic susceptibility testing. The Modified Kirby-Bauer disc diffusion technique was performed using six commonly employed drugs Ampicillin, Co-trimoxazole, ciprofloxacin, ceftriaxone, chloramphenicol, and nalidixic acid[7]. A control strain of E.coli ATCC 25922 was included. The results of susceptibility testing were interpreted using Clinical and Laboratory Standards Institute (2015) recommendation.[8]

RESULTS (age, sex, paed)

Out of 151 samples, a total of 30 isolates of Salmonella species were isolated in 6 months' duration. Out of these 30 isolates, 19 (63%) were Salmonella typhi, whereas 11 (37%) isolates were Salmonella Paratyphi A. There were no isolates of Salmonella Paratyphi B, or C in these 6 months.

Eighty percent of the isolates were resistant to ciprofloxacin whereas 100 percent of the isolates were resistant to Ampicillin. Surprisingly, only 47 percent of the isolates were resistant to chloramphenicol. Ninety-three percent of the isolates were resistant to co trimoxazole. Among third generation cephalosporins, ceftriaxone was susceptible to 10% percent of the isolates.

Out of the 30 samples 18 are in the paediatric age group , ie ages 5 months-18 years. The remaining 7 were from adults out of which 2 were from patients older that 50 years.

The male to female ratio was 18: 11. (1.6:1)

Out of the thirty isolated, 14 (47%) were multidrug resistant. (MDR). Multi Drug resistant is defined as those which are resistant to three or more classes of drugs.

DISCUSSION

The injudicious use of antibiotics has led to an alarming trend in antimicrobial resistance. It was not but 10 years ago, in an article which had taken cases from 1990-1993, which showed that flouroquinolones were 100% sensitive. In this study the MDR Salmonella rate was 67.2%. [9,11]

In another study conducted in India during 2008-2009, the MDR salmonella rate was only 4.7%, which differs significantly from a study in southern India during 2009-2011 claiming to have no MDR salmonella out of its 322 isolates. [10]

In international studies there are also similar

results. One study from Nepal during 2009 shows a sensitivity to ciprofloxacin to be at 94%, which is consistent with the sensivity pattrens of that area in 2009. In Iran the latst information is from 2011, which shows the incidence of enteric fever to be 0.52 per 100,000. There is no information regarding the antibiogram, or resistance rates. [12]

Our study was conducted just 2 years later and shows an alarming rate of 47 %. This number however is much less than the MDR rate of a study conducted in Karachi in 2008-2010, which was 62.6%. This indicated that perhaps MDR rates have decreased with time due to the increased susceptibility of choremphenicol and cotrimoxazole which were resistant in the past. [2,3]

Chloramphenicol susceptibility has improved because we have discontinued this drug in our routine clinical practice.

The results lead to the conclusion that quinolones are no longer the drug of choice in our setup, but in fact if suspected or confirmed, the drug of choice should in fact be third generation cephalosporin. We should have more stringent drug control policy, to keep our MDR rates down. The awareness of this knowledge is important to prevent the inappropriate use of statistically resistant antibiotics. Prescribing antibiotics which are most likely resistant, may lead to treatment failures, increased patient morbidity as well increasing treatment costs.

Table 1: *Antibiotic Susceptibility of all Isolates of Salmonella sp.*

Antibiotic	No's tested	Sensitive	Resistance
Ampicillin	30	0 (0%)	30 (100%)
Cotrimoxazole	30	2(7%)	28(93%)
Chloremphenicol	30	16(53%)	14(47%)
Ciprofloxacin	30	6(20%)	24(80%)
Ceftriaxone	30	27(100%)	3(10%)
Multi-drug resistant strains*	30		14 (47%)

*Resistant to three or more classes of drugs

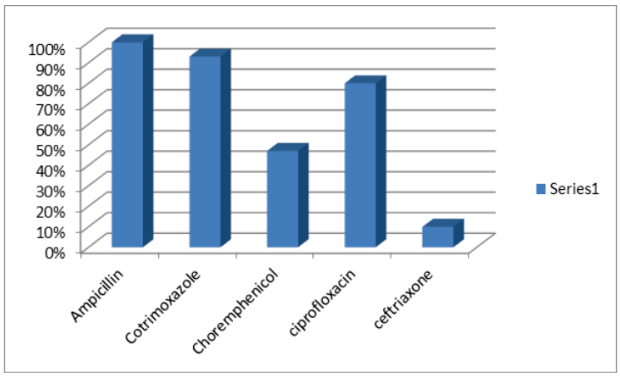

Chart 1

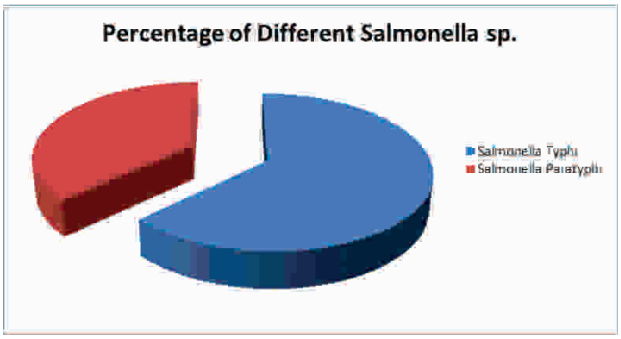

Chart 2

Table 2: *Age distribution*

Age	Number of cases	Percentage
Ages 5 months - 18 years	18	60%
Adults	7	23%
50 years plus	2	6%

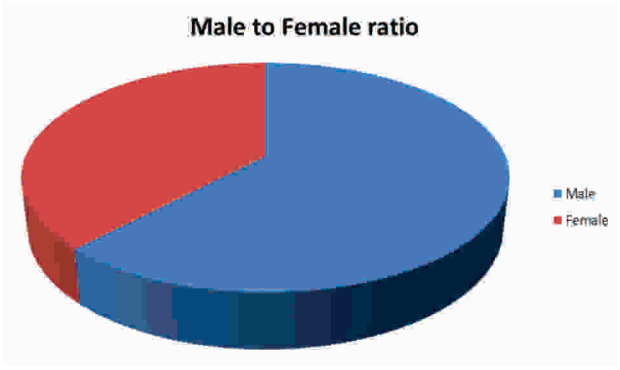

Chart 3

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CORRELATION BETWEEN BODY MASS INDEX AND VITAL SIGNS

Shahroze Wajid, Umair Ashraf, Shahroze Arshad, Muhammad Usman Tahir, Asma Inam, M.Talha Zahid

Shaikh Khalifa Bin Zayed Al-Nahyan Medical and Dental College, Lahore; AzraNaheed Medical College, Lahore; CMH college of Medicine & Dentistry Lahore

Abstract

Objective: The study aims to estimate the correlation between BMI and vital signs (systolic blood pressure, diastolic blood pressure, heart rate (pulse), respiratory rate, temperature)in adolescents to ascertain if changes in BMI cause variations in vital signs.

Design: A cross-sectional study was conducted in 300 male adolescents of Govt. High School Kahna. The sample size was calculated using Epi-Info sample size calculator. The subjects were submitted to a standardized method of measurement of weight, height and vital signs. The data was analyzed in IBM SPSS v21.

Results: The results showed that16 subjects were identified as pre-obese and 141 were labeled as underweight whereas 69 students came out as pre-hypertensive. A significant bivariate Pearson correlation was found ($P<0.05$) between BMI and systolic blood pressure readings, but the correlation between BMI and the other vital signs i.e. diastolic blood pressure, heart rate (pulse), respiratory rate and temperature was insignificant.

Conclusions: There is a significant positive Pearson correlation between BMI and systolic blood pressure (Pearson correlation= +0.113, p-value= 0.04908). There is however, no significant correlation between BMI and the other 4 vital signs i.e. diastolic blood pressure, heart rate (pulse), respiratory rate and temperature. This signifies that childhood obesity is correlated to increased blood pressure and may predispose to hypertension in the future.

Keywords: Obesity, BMI, Hypertension, Vitals, Overweight, Blood Pressure

Adolescence ischaracterized by rapid body growth, with changes in amount of body fat. Childhood and adolescent obesity have been identified as risk factors for obesity in adulthood causing various harmful effects on health later, resulting in an increase in morbidity and mortality.

Obesity is a characterized by high deposition of fat in the body due to increased intake of calories or decreased physical activity.[2,3] The World Health Organization (WHO) classifies overweight and obesity on the basis of body mass index (BMI).[2,3] In 2008, almost 1.46 billion adults of world are overweight and 502 million were obese, whereas 170 million of the children around the world were obese and overweight.[2,4,5] An epidemic of obesity is being experienced by most of the developing and developed countries of the world with some variation found within and between the countries.[6] The increasing industrialization and urbanization in most of the countries has led to changes in diet and behavior in all age groups. The diets are becoming richer in high fat and high-energy nutrients but poorer in micronutrients. In addition, sedentary lifestyles are becoming more prevalent. In many developing countries, chronic under nutrition may co-exist with chronic obesity within the same population.[7] Obese people have been found to have a significantly higher blood pressure than those who are of normal weight or are lean.[8] Obesity represents an important risk factor for cardiovascular diseases. Childhood obesity is often associated with the development of hypertension in the future.[9] The risk factors for cardiovascular

diseases emerge in adolescence and early adulthood[10] and also associated with adiposity in children, reported by many studies.[11] Childhood obesity increases the risk of obesity in adulthood and is associated with cardiovascular diseases, lipid disorders and diabetes mellitus.[12] Obesity also causes an increase in respiratory rate and other vital signs.[13-15]

OBJECTIVE

The objective of this study was to find out the prevalence of both high or low BMI, and its correlation with vital signs variability of adolescents in Government Boys High School Kahna, Lahore.

METHODOLOGY

A cross sectional study was conducted and convenience sampling technique was used. Written consent was taken from the School Principal. Verbal informed consent was taken from the participants of this study.

The population of the school as determined from the School Principal was 2000 students. The Open Epi Sample Size Calculator was used. The calculated sample size was 285 with a 95% confidence level.

Three hundred male students between the ages 13-18 years were recruited from Government High School Kahna, Lahore for one-yearperiodbetween December 2016 to December 2017.Female students or those above 18 years or below 13 years were not included in this study.

A Pro forma was designed to collect the information from each student about his or her name, age, weight, height, blood pressure, heart rate (pulse), respiratory rate and temperature.

The name and age were asked from each student. A weight scale was used to measure the weight in kilograms(kg) and measuring tape to measure the height in centimeters(cm) and blood pressures were recorded in mm of Hg with the help of a Stethoscope and Sphygmomanometer. The right radial pulse was palpated to measure the heart rate by using a wristwatch. The abdominal movements were observed to measure the respiratory rate.

The BMI cutoffs for severely underweight/ moderately underweight/ mildly underweight was<16.0, <17.0 and<18.5 kg/m^2 respectively. The BMI cutoffs for pre-obese/obese as per the WHO classifications were ≥ 25, and ≥30 kg/m^2, respectively.[16]

	Frequency	Percent
Hypotension	2	0.7
Normal	229	76.3
Pre-Hypertensive	69	23.0
Total	300	100.0

The Systolic Blood Pressure cutoffs for hypotension was<90mmHg. The Systolic Blood Pressure cutoffs for pre-hypertension/ stage 1 hypertension/ stage 2 hypertension were >120, >140 and >160 mmHg.[17]

The Diastolic Blood Pressure cutoffs for hypotension was <60mmHg. The Diastolic Blood Pressure cutoffs for pre-hypertension/ stage 1 hypertension/ stage 2 hypertension were>80, >90 and >100mmHg.[17]

The Heart Rate (Pulse) cutoffs for bradycardia and tachycardia were<60 bpm and >100 bpm respectively.[18]

The Respiratory Rate cutoffs for Brachypnea (Hypoventilation) and Tachypnea (Hyperventilation) were <12 and >20 breaths per minute respectively.[18] While the Temperature cutoffs for Hypothermia and Hyperthermia were<95°F and >99.5°F respectively.

The data was collected by measuring the above stated parameters for 5 hours daily for three consecutive days on a pre-printed Pro forma provided by IFMSA and was entered and analyzed in IBM SPSS Statistics Ver.21.

RESULTS

BMI

The results showed that out of 300 subjects, 32

	Frequency	Percent
Severe Underweight	32	10.7
Moderately Underweight	37	12.3
Mildly Underweight	72	24.0
Normal	138	46
Pre-Obese	21	7.0
Total	300	100.0

(10.7%) were severely underweight whereas 37 (12.3%) were moderately underweight and 72 (24.0%) were mildly underweight. 138 subjects (46%) were of normal weight and 21 subjects (7%) were pre-obese.

SYSTOLIC BLOOD PRESSURE

2 subjects (0.6%) were hypotensive. 229 subjects (76.3%) presented with normal systolic blood pressure and 69 subjects (23%) were pre-hypertensive.

From 32 subjects that fall under severe underweight category, 30 were with normal blood pressure whereas one was pre-hypertensive and one was

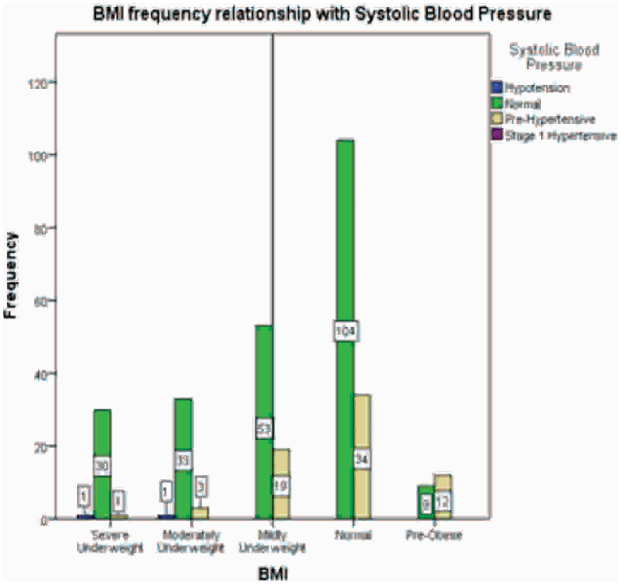
		BMI-Systolic Blood Pressure Crosstab			
		Hypotension	Normal	Pre-Hyper-tensive	Total
BMI	Severe Underweight	1	30	1	32
	Moderately Underweight	1	33	3	37
	Mildly Underweight	0	53	19	72
	Normal	0	104	34	138
	Pre-Obese	0	9	12	21
Total		2	229	69	300

hypotensive. From 37 subjects that fall under moderately underweight category 33 were with normal blood pressure. 3 students were pre-hypertensive and 1 student was hypotensive. Out of 72 subjects that fall under mildly underweight category, 53 subjects were with normal blood pressure and 19 were pre-hypertensive. Regarding the weight parameters, 138 subjects that fall under normal weight category. 104 were with normal blood pressure whereas 34 subjects were pre-hypertensive. From 21 subjects that fall under pre-obese category, 9 subjects were with normal blood pressure. 12 subjects were pre-hypertensive.

There was a significant correlation between categorical data of BMI and Systolic Blood Pressure (Pearson Correlation Coefficient= 0.113, $p<0.05$).

DIASTOLIC BLOOD PRESSURE

Measuring the diastolic blood pressure, 1 subject (0.3%) was hypotensive while 253 subjects



	Frequency	Percent
Hypotensive	1	0.3
Normal	253	84.3
Pre-Hypertensive	16	5.3
Stage 1 Hypertensive	25	8.3
Stage 2 Hypertensive	5	1.7
Total	300	100.0

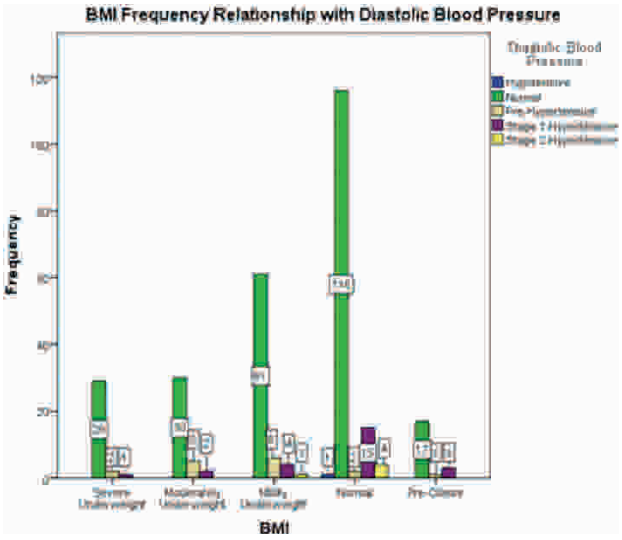
(84.3%) were with normal diastolic blood pressure. 16 subjects (5.3%) were pre-hypertensive while 25 subjects (8.3%) were stage 1 hypertensive and 5 subjects (1.7%) were Stage 2 hypertensive.

From 32 subjects that fall under severe underweight category, 29 were with normal blood pressure. 2 were pre-hypertensive. 1 was stage 1 hypertensive. From 37 subjects that fall moderately underweight category, 30 were with normal blood pressure whereas 5 were pre-hypertensive and 2 were stage 1 hypertensive. From 72 subjects that fall under mildly underweight category 61 subjects were with normal blood pressure. 6 were pre-hypertensive while 4 were stage 1 hypertensive and 1 was stage 2 hypertensive. From 138 subjects that fall under normal weight

category 1 subject was hypotensive. 116 were with normal blood pressure. 2 subjects were pre-hypertensive. 15 were stage 1 hypertensive. 4 were stage 2 hypertensive. From 21 subjects that fall under pre-obese category 17 subjects were with normal blood pressure. 1 subject was pre-hypertensive. 3 subjects were stage 1 hypertensive. There was an insignificant correlation between the categorical data of BMI and Diastolic Blood Pressure (Pearson Correlation Coefficient= 0.067, p>0.05).

HEART RATE

1 subject (0.3%) had bradycardia. 293 subjects (97.7) had normal pulse rate. 6 subjects (2 %) had



	Frequency	Percent
Bradycardia	1	0.3
Normal	293	97.7
Tachycardia	6	2.0
Total	300	100.0

tachycardia.

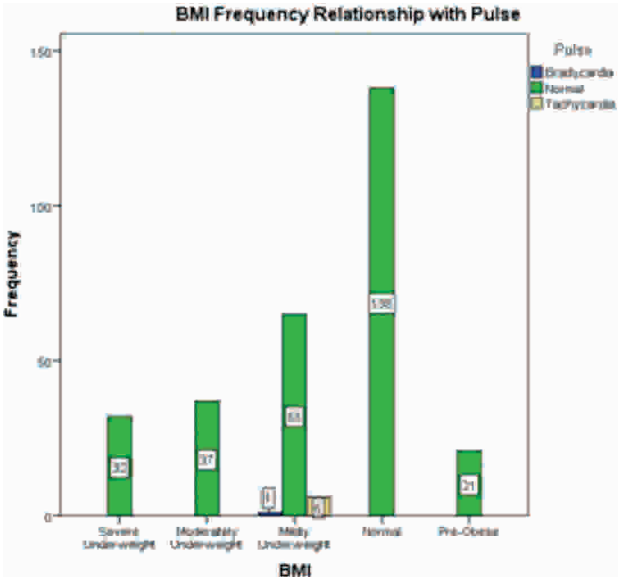
From 32 subjects that fall under severe under-weight category all 32 subjects had normal pulse rate. From 37 subjects that fall under moderately underweight category all 37 subjects had normal pulse rate. From 72 subjects that fall under mildly underweight category 1 subject had bradycardia. 65 subjects were with normal pulse rate. 6 subjects had tachycardia. From 138 subjects that fall under normal weight category all 138 subjects had normal pulse rate. From 21 subjects that fall under pre-obese category all 21 subjects had normal pulse rate.

		BMI-Systolic Blood Pressure Crosstab			
		Bradycardia	Normal	Tachycardia	Total
BMI	Severe Underweight	0	32	0	32
	Moderately Underweight	0	37	0	37
	Mildly Underweight	1	65	6	72
	Normal	0	138	0	138
	Pre-Obese	0	21	0	21
Total		**1**	**293**	**6**	**300**

There was an insignificant correlation between the categorical data of BMI and Heart rate (Pearson Correlation Coefficient= -0.108, p>0.05).

RESPIRATORY RATE

3 subjects (1%) were suffering from hypo-



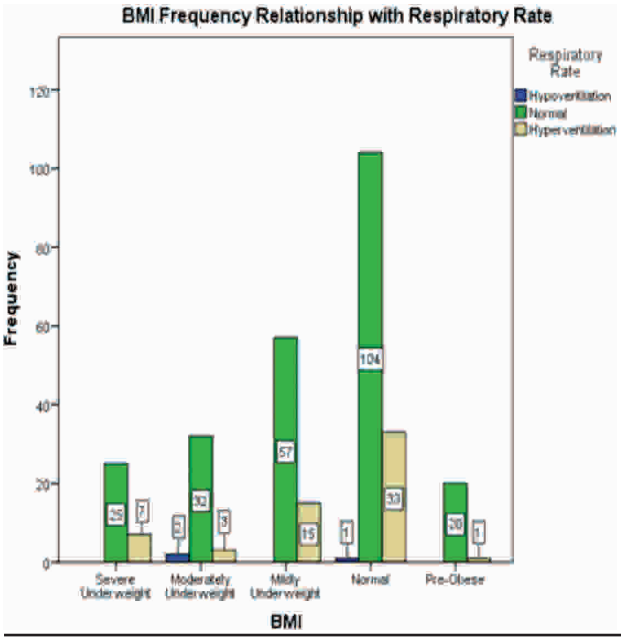
ventilation. 238 subjects (79.3%) had a normal respiratory rate. 59 subjects (19.7%) were suffering from hyperventilation.

	Frequency	Percent
Hypoventilation	3	1.0
Normal	238	79.3
Hyperventilation	59	19.7
Total	300	100.0

		BMI-Respiratory Rate Blood Pressure Crosstab			
		Hypoventi-lation	Normal	Hyperven-tilation	Total
BMI	Severe Underweight	0	25	7	32
	Moderately Underweight	2	32	3	37
	Mildly Underweight	0	57	15	72
	Normal	1	104	33	138
	Pre-Obese	0	20	1	21
Total		**3**	**238**	**59**	**300**

From 32 subjects that fall under severe underweight category all 25 subjects had normal respiratory rate. 7 subjects had hyperventilation. From 37 subjects that fall under moderately underweight category 2 subjects had hypoventilation. 32 subjects had normal respiratory rate.3 subjects had hyperventilation. From 72 subjects that fall under mildly underweight category 57 subjects were with normal respiratory rate. 15 subjects had hyperventilation. From 138 subjects that fall under normal weight category 1 subject had hypoventilation. 104 subjects had normal respiratory rate. 33 subjects had hyperventilation. From 21 subjects that fall under pre-obese category 20 subjects had normal respiratory rate. 1 subject had hyperventilation.

There was an insignificant correlation between the categorical data of BMI and Respiratory Rate (Pearson Correlation Coefficient= -0.026, p>0.05).



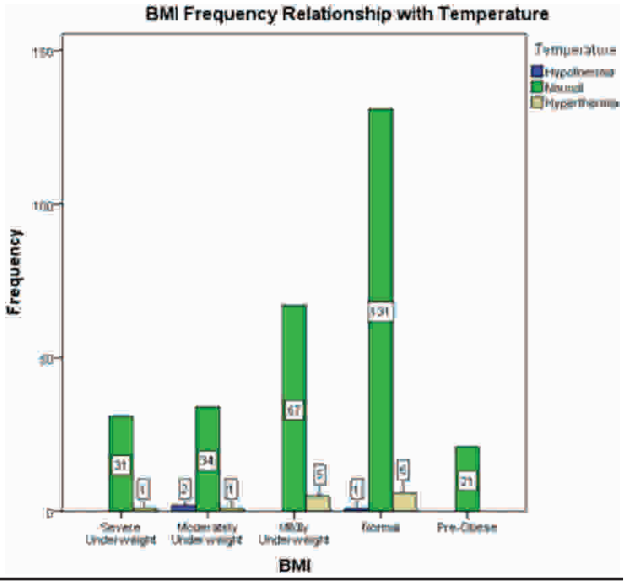
TEMPERATURE

	Frequency	Percent
Hypothermia	3	1.0
Normal	284	94.7
Hyperthermia	13	4.3
Total	300	100.0

3 subjects (1%) were hypothermic. 284 subjects (94.7%) had a normal body temperature. 13 subjects (4.3%) were hyperthermic.

		BMI-Temperature Crosstab			
		Hypother-mia	Normal	Hyperther-mia	Total
BMI	Severe Underweight	0	31	1	32
	Moderately Underweight	2	34	1	37
	Mildly Underweight	0	67	5	72
	Normal	1	131	6	138
	Pre-Obese	0	21	0	21
Total		**3**	**284**	**13**	**300**

From thirty two subjects that fall under severe underweight category 31 subjects had normal body temperature. 1 subject was hyperthermic. From 37 subjects that fall under moderately underweight category 2 subjects were hypothermic. 34 subjects had normal body temperature. 1 subject was hyperthermic. From 72 subjects that fall under mildly underweight category 67 subjects had normal body temperature. 5 subjects were hyperthermic. From 138 subjects that fall under normal weight category 1



subject was hypothermic 131 subjects had normal body temperature. 6 subjects were hyperthermic. From 21 subjects that fall under pre-obese category all 21 subjects had normal body temperature.

There was an insignificant correlation between the categorical data of BMI and Temperature (Pearson Correlation Coefficient= -0.073, p>0.05).

Significance Tests (P-value)

	BMI	
	Pearson Correlation Coefficient	P-Value
Systolic Blood Pressure	.113	.049
Diastolic Blood Pressure	.067	.247
Heart Rate (Pulse)	-.108	.061
Respiratory Rate	-.026	.656
Temperature	-.073	.209

The bivariate Pearson correlation test was used to assess the significance of correlation between BMI and Vital Signs. A p-value less than 0.05 denotes significance between two variables.

The results show that there is a significant positive correlation between BMI and Systolic Blood Pressure (Pearson correlation = +0.113, p-value = 0.0498).There is however, no significant correlation between BMI and the other 4 vital signs i.e. Diastolic Blood Pressure, Pulse, Respiratory Rate and Temperature.

DISCUSSION

This study demonstrates the correlation of Body Mass Index with the Vital Signs i.e. Systolic Blood Pressure, Diastolic Blood Pressure, Heart Rate, Respiratory Rate and Temperature. The hypothesis was to demonstrate raised vital signs on high BMI. The null hypothesis says that there is no significant correlation between BMI and Vital Signs. This study shows a significant Pearson correlation between BMI and Systolic Blood Pressure ($p<0.05$), so the null hypothesis is rejected. Nevertheless, the correlation between BMI and Heart Rate, Pulse and Temperature is insignificant ($p>0.05$), so the null hypothesis is accepted for these three variables.

Many previous studies[8][9][10][11][19][20][21, 22][23] have shown that obese children had significantly higher Blood Pressure than nonobese children. The similarity between the results of this study and above documented studies signifies that there must be a positive correlation between BMI and Blood Pressure.

There is an incidental finding in this study that signifies another major issue in our society. This study was conducted in a school for lower or lower-middle class children where, out of 300 subjects, 141 (47%) were underweight. 138 (46%) children were of normal weight and 21 children(7%) were pre-obese. This shows that there is a very high ratio (47%) of underweight children among the selected population of lower-middle class children compared to the global average prevalence of 13.5% underweight children according to UNICEF, WHO[24]. This finding points to the fact that more poverty leads to greater prevalence of low weight among children. A study[23] in Hong Kong, China shows that lower family socioeconomic statusis associated with higher risk of obesity and hypertension in childhood, whereas lower neighborhood socioeconomic status is associated with higher risk in underweight, overweight, and obesity.

The increasing prevalence worldwide has led to more attention being given to obesity in childhood and its long-term effects in adults. Many studies have been performed to assess the short- and long-term effects of childhood obesity on health. As our study proves a significant relationship between BMI and Systolic and Diastolic Blood Pressure, so, in application of this research, we can spread awareness among the population about the effects of overweight on blood pressure, so as to guide them about the risks of developing hypertension in the future.

This study may be compared to other similar studies and can further improve by continuing as a prospective cohort study on the same patients. The study results can be compared between students of government and private schools or between males and females. Different other techniques to assess child malnutrition e.g. Triceps skin fold thickness, blood sugar levels, blood vitamin levels etc. can also be used to analyze the various aspects of malnutrition in the community.

CONCLUSION

There is a significant positive Pearson correlation between BMI and systolic blood pressure (Pearson correlation= +0.113, p-value= 0.04908). There is however, no significant correlation between BMI and the other 4 vital signs i.e. diastolic blood pressure, heart rate, respiratory rate and temperature. This signifies that since childhood obesity is correlated to increased blood pressure, it may predispose to hypertension in the future.

The government should take appropriate steps to guide and aware the population about good dietary habits and an active lifestyle, so as to minimize the prevalence of overweight and underweight and to control the incidence and prevalence of hypertension.

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ASSOCIATION OF HYPOMAGNESEMIA WITH MYOCARDIAL INFRACTION

Ahmed Muqeet[1], Noor Dastgir[2], Arslan Masood[3]

[1]Assistant Professor, 2Assistant Professor, 3Associate Professor
Department of Cardiology Jinnah Hospital, Lahore

Abstract

Background: Hypomagnesaemia is an independent predictor of CHD in both genders. Low serum magnesium causes endothelial damage that accelerates the atherosclerotic process leading to ACS. Evidence links significant low serum magnesium to CHD in patient with Acute Myocardial Infarction (AMI) versus control.

Objective: Objective of this study was to find association between hypomagnesaemia and myocardial infarction.

Methodology: After approval of synopsis, 178 (89 cases/ 89 controls) patients who fulfill the inclusion criteria, were enrolled in the study. Informed consent was obtained from all patients and the study protocol was explained. Data was collected in a structured questionnaire (proforma) containing background information like age, sex and serum magnesium level. Under aseptic conditions, venous blood samples were obtained from patients at the time of presentation in hospital. Serum magnesium level was measured by using standard chemical analyzer of Allama Iqbal Medical College. Effect modifiers like history of hypertension, BMI>30kg/m^2 at time of presentation were recorded additionally to account for their effect. Hypomagnesaemia was recorded in cases and controls as per operational definition. Data was collected by the researcher himself on a pre-designed proforma.

Results: In our study, out of 178 patients (89 in cases and 89 in controls), 42.70%(n=38) in cases and 32.58%(n=29) in controls were between 20-40 years of age while 57.30%(n=51) in cases and 67.42%(n=60) were between 41-60 years of age, mean + sd was calculated as 44.22+9.08 in cases and 45.82+8.54 years in controls, 51.69%(n=46) in cases and 44.94%(n=40) in controls were male while 48.31%(n=43) in cases and 55.06%(n=49) in controls were females, mean serum magnesium level were calculated as 1.12+0.30 mg/dl in cases and 1.46+0.42 mg/dl in controls, association between hypomagnesaemia and myocardial infarction was recorded and it shows that 89.89%(n=80) in cases and 48.31%(n=43) in controls had hypomagnesemia, odds ratio was calculated as 9.50 showing a significant difference.

Conclusion: | We concluded that there is a strong association between hypomagnesaemia and myocardial infarction. However, some-other trials should also be conducted to validate our findings. s

Keywords: | Myocardial infarction. | Hypomagnesaemia.

Cardiovascular diseases, including myocardial infarction (MI), are among the leading causes of deaths worldwide. Myocardial infarction is on the rise globally and more so in developing countries.[1,2] Lower serum magnesium levels may cause atrial fibrillation as shown in a study where atrial fibrillation increased by 54% in the lowest quartile compared to the highest quartile of serum magnesium (Mg)[3] leading to further morbidity. Mg is the second most abundant intracellular cation in the body.[4] Approximately 40% of the Mg contained in the adult human body is present in muscles and soft tissue, about 1% in the extracellular fluid, and rest in the skeleton.[5] The plasma Mg level is maintained remarkably constant in healthy individuals. Mg is an essential co-factor of more than 300 enzymes, including sodium potassium adenosine triphosphatase (Na-K ATPase), an enzyme that influences

cardiac irritability.[6-9]

One study showed that low serum magnesium levels may be triggering mechanisms for ischemic heart disease, arrhythmias after open heart surgery, serious arrhythmias such as Torsades de Pointes (TdP), and the negative feedback in congestive heart failure[4]. Supplemental and therapeutic Mg infusions have been reported controversially to reduce the mortality in acute myocardial infarction.[5] Magnesium supplementation improves myocardial metabolism, inhibits calcium accumulation and myocardial cell death; it improves vascular tone, peripheral vascular resistance, afterload and cardiac output, reduces cardiac arrhythmias and improves lipid metabolism.[8] For patients with myocardial infarction, after adjusting for age, positive family history, smoking status, hypertension, hypercholesterolemia, and diabetes at baseline, the risk of major adverse cardiac events was 8 fold higher for patients with quartile 1 than 4 of Mg level (95% confidence interval 1.7-38.75; P<0.01).[6] In a Bangladeshi study the frequency of hypomagnesaemia in myocardial infarction cases was 86.66% and in controls was 58.06%.[10]

METHODS

This case control study was carried out over a period of six months and included 178 patients (sample size of 178 was calculated keeping a level of significance and 80% power of study, taking the expected percentage of hypomagnesaemia in myocardial infarction cases 86.66% and in controls 58.06%).[10] The study included patients of either gender between 20 and 60 years of age presenting with chest pain and diagnosed as myocardial infarction (according to 3rd universal definition of M.I. i.e., Elevated Troponin levels with one of either chest pain, ST segment elevations in two contagious leads, new wall motion abnormalities or detection of thrombus in coronary artery on angiography) presenting within 6 hours of start of symptoms determined by history. Age and gender matched relatives of the patients were included as controls. Exclusion criteria were smoking, diabetes, recent drug intake changing serum magnesium level e.g. multivitamins, calcium supplements and diuretics like hydrocholthiazide, history of chronic liver disease diagnosed by elevated ALT more than 100 IU/ml, end stage renal disease (estimated creatinine clearance < 10 mL/min) and diagnosed cases of chronic obstructive pulmonary disease.

Under aseptic conditions, venous blood samples were obtained from patients at the time of presentation in hospital. Serum magnesium level was measured by using standard chemical analyzer using flame photometer equipment in Allama Iqbal Medical College pathology laboratory. Effect modifiers like history of hypertension, BMI > 30kg/m^2 at time of presentation were recorded additionally to cater their effect. A cutoff level of less than 1.7 mg/dl was used to define hypomagnesemia. Odd`s ratio was calculated for association of hypomagnesaemia with myocardial infarction. Data was stratified for age, gender, hypertension, socioeconomic status, and BMI as potential effect modifiers and post stratification Odd`s ratios were calculated.

RESULTS

A total of 178 cases fulfilling the inclusion/exclusion criteria were enrolled to find association between hypomagnesaemia and myocardial infarction.

Age distribution of the patients was done showing that 42.70%(n=38) in cases and 32.58% (n=29) in controls were between 20-40 years of age while 57.30%(n=51) in cases and 67.42%(n=60) in controls were between 41-60 years of age, mean+sd was calculated as 44.22+9.08 in cases and 45.82+ 8.54 years in controls.

Patients were distributed according to gender, it shows that 51.69%(n=46) in cases and 44.94% (n=40) in controls were male while 48.31%(n=43) in cases and 55.06%(n=49) in controls were females.

Mean serum magnesium level were calculated as 1.12+0.30 mg/dl in cases and 1.46+0.42 mg/dl in

Stratification for Association of Hypomagnesemia with Regards to Age, Gender, H/O Hypertension, Socioeconomic Class & Body Mass Index

AGE: 20-40				MALE				Hypertension				Poor & Middle Class				BMI <30			
	Association		OR		Association		OR		Association		OR		Association		OR		Association		OR
Group	Yes	No		Group	Yes	No		Group	Yes	No		Group	Yes	No		Group	Yes	No	
Cases	35	3		Cases	43	3		Cases	41	7		Cases	44	3		Cases	36	5	
Control	13	16	14.35	Control	25	15	8.6	Control	27	12	2.6	Control	28	19	9.95	Control	26	22	6.09

AGE: 41-60				FEMALE				No Hypertension				Higher Class				BMI >30			
	Association		OR		Association		OR		Association		OR		Association		OR		Association		OR
Group	Yes	No		Group	Yes	No		Group	Yes	No		Group	Yes	No		Group	Yes	No	
Cases	45	6		Cases	37	6		Cases	29	12		Cases	36	6		Cases	44	4	
Control	30	30	7.5	Control	18	31	10.62	Control	16	34	5.13	Control	15	27	10.8	Control	20	21	11.55

Table 4: *Association Between Hypomagnesaemia and Myocardial Infarction (n=178)*

Hypomagnesemia	Cases (n=89)		Controls (n=89)	
	No. of patients	%	No. of patients	%
Yes	80	89.89	43	48.31
No	9	10.11	46	51.69
Total	**89**	**100**	**89**	**100**

Odds ratio	9.5090
95 % CI:	4.2522 to 21.2648
z statistic	5.485
Significance level	P < 0.0001

controls.

Association between hypomagnesaemia and myocardial infarction was recorded and it shows that 89.89% (n=80) in cases and 48.31%(n=43) in controls had hypomagnesemia while 10.11%(n=9) in cases and 51.69%(n=46) in controls had no findings of the morbidity, odds ratio was calculated as 9.50 showing a significant difference.

The data was stratified for age, gender, H/o, hypertension, socioeconomic status, and BMI as potential effect modifiers. OR > 1 was considered significant.

DISCUSSION

Hypomagnesaemia is an independent predictor of CHD in both genders. Low serum magnesium causes endothelial damage that accelerates the atherosclerotic process leading to ACS. Evidence links significantly low serum magnesium to CHD in patient with Acute Myocardial Infarction (AMI) versus controls.

In our study, out of 178 cases (89 in cases and 89 in controls), 42.70%(n=38) in cases and 32.58% (n=29) in controls were between 20-40 years of age while 57.30%(n=51) in cases and 67.42%(n=60) were between 41-60 years of age, mean+sd was calculated as 44.22+9.08 in cases and 45.82+8.54 years in controls, 51.69%(n=46) in cases and 44.94% (n=40) in controls were male while 48.31% (n=43) in cases and 55.06%(n=49) in controls were females, mean serum magnesium level were calculated as 1.12+0.30 mg/dl in cases and 1.46+0.42 mg/dl in controls, association between hypomagnesaemia and myocardial infarction was recorded and it shows that 89.89%(n=80) in cases and 48.31%(n=43) in controls had hypomagnesemia, odds ratio was calculated as 9.50 showing a significant difference.

The findings of our study are in agreement with a Bangladeshi study where the frequency of hypomagnesaemia in myocardial infarction cases was 86.66% and in controls was 58.06%.[10]

A cross-sectional cohort study has shown inverse 136 Ischemic Heart Disease association between serum magnesium and carotid intima-media thickness.[11] Low serum magnesium causes endothelial damage that accelerates the atherosclerotic process leading to ACS. Evidence links significant low serum magnesium to CHD in patient with Acute Myocardial Infarction (AMI) versus control.[12-14] A cohort of 15,792 middle aged subjects were assessed over a four to seven year period as part of the Atherosclerosis Risk in Communities (ARIC) study.78 The relative risk of CHD across quartiles of serum magnesium was 1.0 (in the lowest quartile), 0.92, 0.48 and 0.44. Both men and women who developed CHD had lower mean baseline serum magnesium concentration than the disease-free controls.

Jaffery and others[15] in a descriptive case series study evaluated the frequency of hypomagnesemia in patients with acute myocardial infarction they recorded that out of 100 diabetic patients, 77 were males and 23 patients were females. The mean age and standard deviation of patients of male and female was 54.78 Â± 8.82 (SD) and 53.64 Â± 10.82 (SD), respectively. The mean Â± SD for serum magnesium in overall subjects was 1.24 Â±0.48. Regarding the type of AMI inferior wall in 22 (29%), lateral wall in 17 (22%), anteroseptal in 12 (16%), anterolateral -V1 in 07(09%), right ventricular in 10 (13%) and posterior wall in 07 (09%). The mean duration of acute MI in male and female population was 8.71Â±6.73 hours and 17.70Â±14.57 hours ($p<0.01$) where as the mean duration of acute MI in hypomagnesemic and normomagnesemic patient was 5.16Â±2.49 hours and 26.60Â±8.27 ($p = 0.02$) respectively. The mean serum magnesium level in male as well as female population was 1.32 Â±0.21 mg/dl and 1.46Â± 0.53 mg/dl $p = 0.05$, respectively. Regarding the hypomagnesemia in male and female population was 34(75.6%) and 16(53.3%) $p=0.04$, respectively. The hypomagnesemia was more predominant in inferior 18(36.0%) and lateral 16 (32.0%) wall MI, they concluded that the hypomagnesemia was observed in patients with acute myocardial infarction with statistical significance.

The findings of our study is helpful in establishing baseline data for formulating guidelines for periodic determination of magnesium levels and recommendation of appropriate magnesium supplements for patients at risk of MI. This study will also help to reduce mortality and morbidity associated with lower levels of magnesium in these patients.

CONCLUSION

- We concluded that there is a strong association between hypomagnesaemia and myocardial infarction. However, some other larger trials should also be conducted to validate our findings.

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SERUM VITAMIN D LEVELS IN PAKISTANI MALE PATIENTS WITH GUILLAIN BARRE SYNDROME

Kashif Aziz Ahmad, Sohaib Akbar[1], Rizwan Ahmad[2], Muhammad Maqsood[3], Sheraz Anjum[4], Muhammad Imran Hasan Khan[5], Asif Khurshid[6]

[1]Assistant Professor,[2]Medical officer, Lahore General Hospital; [2]Senior Registrar, Lahore General Hospital; [3]Senior Registrar, Lahore General Hospital; [4]Medical Officer, Lahore General Hospital; [5]Hospital Pharmacist, Lahore General Hospital; [6]Asssociate Professor of Medicine, Ameer-ud-Din Medical College / Postgraduate Medical Institute Lahore General Hospital, Lahore

Abstract

Objectives: To determine serum vitamin D levels of male patients of Guillain Barre syndrome (GBS) and compare them with those of healthy controls.

Materials and Methods:

Study Design: Comparative cross-sectional study

Settings: Department of Medicine, Ameer-ud-Din Medical College/ Postgraduate Medical Institute, Lahore General Hospital, Lahore, Pakistan

Study Duration: January 2018 to December 2018.

Data Collection: Male GBS patients were enrolled in the study and healthy subjects who volunteered for the study were recruited as control group. Serum vitamin D levels were measured and compared between the two groups. Independent t-test was used to see the statistical differences in the vitamin D levels of the two study groups with p-value < 0.05 considered statistically significant.

Results: Fifty patients were recruited in each group. The mean age of the GBS patients was 36.7 ± 11.5 (range: 16 – 58) years whereas that of control group was 33.6 ± 7.9 (range: 18 – 50) years. The cause of GBS was preceding respiratory infection in 22 (44.0%) cases and preceding gastrointestinal infection in 28 (56.0%) cases. The mean vitamin D level in GBS patients and healthy participants was 9.62 ± 4.5 ng/dL and 38.7 ± 11.6 ng/dL respectively (p-value < 0.0001). We found that 41 (82.0%) of the GBS patients had severely low vitamin D levels below 12 ng/dL whereas none in the healthy group had vitamin D deficiency. Seven (14.0%) GBS patients had borderline vitamin D levels (12 – 20 ng/dL) whereas only two (4.0%) GBS patients had normal vitamin D levels (>20 ng/dL) respectively. History of smoking was significantly associated with lower vitamin D levels in GBS patients (p-value = 0.001).

Conclusion: Vitamin D levels are significantly low in GBS patients as compared with healthy normal individuals. Smoking was significantly associated with low levels of vitamin D in GBS patients.

Keywords: Vitamin D levels, Guillain Barre Syndrome, Smoking, Deficiency

Guillain Barre syndrome (GBS) is an auto-immune disease associated with an ascending paralysis producing a constellation of neurological signs and symptoms.[1] Immunologically, it is part of a spectrum of demyelinating peripheral neuropa-thies that occur due to abnormalities of axonal transmission which occur secondary to immune mediated injuries. Various researches have shown upregulation of pro-inflammatory T-helper lympho-cytes and CD4+ cells which cause neuronal injury in GBS.[2,3]

Vitamin D has shown to have neuro-protective effect on the neuronal tissue by acting on vitamin D receptors in the nuclei of various immune cells.[4]

Correspondence: Dr. Kashif Aziz Ahmad, Assistant Professor of Medicine, Ameer-ud-Din Medical College / Postgraduate Medical Institute, Lahore General Hospital, Lahore, Email: drkashifaziz@yahoo.com

Vitamin D causes suppression of pro-inflammatory lymphocytes and causes upregulation of various regulatory and inhibitory T-cells.[5] Deficiency of vitamin D has recently been linked to various immune mediated auto-immune disorders including multiple sclerosis, myasthenia gravis, myopathies, systemic lupus erythematosus, rheumatoid arthritis, type 1 diabetes mellitus, and narcolepsy.[5–11] All these diseases are characterized by abundance of autoreactive T- cells. Some researchers have attributed steroid treatment for these diseases to be the cause of vitamin D deficiency in these patients.[12] A recent study showed that administration of vitamin D therapy in myasthenia patients significantly improved the symptoms of fatigue in these patients confirming the role of vitamin D in peripheral neuropathies.[12]

Though most of the research today focuses on testing advanced immune regulatory agents to treat autoimmune peripheral neuropathies, role of vitamin D itself has received scant attention in the medical literature. Vitamin D levels in an individual are dependent on multiple factors including dietary habits, sunlight exposure, latitude and other co-morbidities. Though Pakistan is located near the equator and receives plenty of sunlight, vast majority of our population is endemically low in Vitamin D levels.[13] Since female patient of our country has significantly low vitamin D levels, we included only male population in our study to prevent any gender bias in the study[(14)]. We intended to conduct this study with the objective to determine the differences in the vitamin D levels between male patients suffering from GBS and their healthy age matched controls. We conducted a detailed literature search on Google Scholar, PubMed, PakMedinet, EMBASE and Cochrane library but found no previous published reports on the subject from our country making this study a very useful addition to the medical literature.

METHODS

It was a comparative cross-sectional study conducted in Department of Internal Medicine of Ameer-ud-Din Medical College and Lahore General Hospital, Lahore from January 2018 to December 2018. The study was conducted after obtaining formal approval of its synopsis from the Ethical Review Committee of the same institute and adhered to the principles of ethical medical practice as laid down in Declaration of Helsinki 2011. An informed written consent was obtained from all study participants.

Patients were diagnosed as having GBS after detailed clinical evaluation and neurological criteria for diagnosis of GBS as laid down in European Federation of Neurological Societies guidelines.[15] To add a control group in our study for comparison of vitamin D levels, we also recruited healthy male attendants of our patients and checked their vitamin D levels. All samples were collected and stored in EDTA before being sent for detailed analysis by the Chemical Pathology of Lahore General Hospital. We divided the vitamin D levels into 3 categories: normal (> 20 nm/dL), borderline (12 – 20 ng/dL) and low (< 12 ng/dL).

All the data were entered and analyzed using Statistical Package for Social Sciences (SPSS, IBM Statistics, Chicago, IL, USA Version 25.0). The categorical variables were presented as frequencies and percentages whereas the nominal variables were calculated as mean ± SD. There were two groups in the study: 1) patients with GBS and 2) heathy normal age matched controls. We used independent sample t-test to evaluate the statistical significance between the two groups. A p-value of < 0.05 was considered statistically significant.

RESULTS

There were one hundred subjects in the study with 50 male individuals in each arm of the study. The mean age of the patients in the GBS group was 36.7 ± 11.5 (range: 16 – 58) years whereas the mean age of the control (healthy) group was 33.6 ± 7.9 (range: 18 – 50) years. The cause of GBS was

preceding respiratory infection in 22 (44.0%) cases and preceding gastrointestinal infection in 28 (56.0%) cases.

The mean vitamin D level in patients with GBS and healthy participants was 9.62 ± 4.5 ng/dL and 38.7 ± 11.6 ng/dL respectively (p-value < 0.0001) (table 1).

We evaluated the number and percentage of patients in different sub-categories of vitamin D levels. We found that 41 (82.0%) of GBS patients had severely low vitamin D levels below 12 ng/dL whereas none in the healthy group had vitamin D deficiency. Similarly, 7 (14.0%) and 2 (4.0%) individuals with GBS had borderline (12 – 20 ng/dL) and normal vitamin D levels (>20 ng/dL) respectively. On the contrary, 50 (100.0%) healthy participants had normal vitamin D levels (>20ng/dL) (table 1). All the differences between these values were statistically significant with p < 0.0001.

Table 1: Mean Age, Vitamin D Levels and Distribution of Study Population into Various Vitamin D Level Subgroups

		Study Groups		Total
		Cases (GBS)	Controls (Healthy)	
Age (years)	Mean ± SD	36.8 ± 11.5	33.6 ± 7.9	
Vitamin D Levels (ng/dL)	Mean ± SD	9.6 ± 4.5	38.7 ± 11.6	
Vitamin D Levels Breakdown:				
Severe Vitamin D Deficiency (< 12 ng /dl)	Count (n)	41	0	41
	%	82.0%	0.0%	41.0%
Borderline Vitamin D Level (12 - 20 ng / dl)	Count (n)	7	0	7
	%	14.0%	0.0%	7.0%
Normal Vitamin D Levels (> 20 ng /dl)	Count (n)	2	50	52
	%	4.0%	100.0%	52.0%
Total	Count (n)	50	50	100
	%	100.0%	100.0%	100.0%

We also compared the effect of smoking on vitamin D levels in our study population. We found that history of smoking was equally distributed amongst healthy participants with 25 (50.0%) subjects being smokers and 25 (50.0%) subjects being non-smokers. On the other hand, 20 (40.0%) patients with GBS were smokers and 30 (60.0%) patients were non-smokers (table 2). The smoking status was significantly different between the study groups statistically (P = 0.001).

DISCUSSION

The primary objective of the study to compare vitamin D levels in patients with GBS and healthy controls was successfully met. Patients with GBS developed the disease either because of preceding respiratory or gastrointestinal disease. We found that vitamin D levels were significantly low in patients with GBS as compared with healthy normal controls. History of smoking was associated with significantly lower levels of vitamin D in patients with GBS.

Table 2: Relationship between Smoking and Vitamin D Levels in Gbs Patients and Healthy Controls

Smoker	Vitamin D Levels		Study Groups		Total
			Case (GBS)	Control (Healthy)	
Yes	Vitamin D deficiency (< 12 ng /dl)	Count (n)	17	0	17
		%	85.0%	0.0%	37.8%
	Borderline Vitamin D Level (12-20 ng / dl)	Count (n)	3	0	3
		% within Group	15.0%	0.0%	6.7%
	Normal Vitamin D Level (> 20 ng /dl)	Count (n)	0	25	25
		% within Group	0.0%	100.0%	55.6%
	Total	Count (n)	20	25	45
		% within Group	100.0 %	100.0%	100.0 %
No	Vitamin D deficiency (< 12 ng /dl)	Count (n)	24	0	24
		% within Group	80.0%	0.0%	43.6%
	Borderline Vitamin D Level (12 - 20 ng / dl)	Count (n)	4	0	4
		% within Group	13.3%	0.0%	7.3%
	Normal Vitamin D Level (>20 ng /dl)	Count (n)	2	25	27
		% within Group	6.7%	100.0%	49.1%
	Total	Count (n)	30	25	55
		% within Group	100.0 %	100.0%	100.0 %

Vitamin D has been shown to upregulate the immuno-protective T-lymphocytes by causing increased production of their anti-inflammatory products expressed on the nuclear receptors. Immu-

nologically GBS is caused by excessive production of Th1-cytokines which provoke and aggravate neuronal inflammation at various sites producing characteristic neuropathies seen in GBS. Vitamin D greatly increases the production of Th2-immune cells which help in the recovery of patients from various immune mediated neuropathies including GBS.[16] Similarly, some studies have attributed symptoms of peripheral neuropathy including paresthesias and numbness to low levels of vitamin D in diabetic patients.[17] A proposed mechanism for vitamin D deficiency in autoimmune neuropathies is the corticosteroid treatment.[18] However, exact mechanism explaining how this occurs still remains to be explored and described.

A recent study by Elf et al showed that patients with immune mediated peripheral neuropathy and motor neuron disease exhibited significantly lower levels of serum vitamin D levels as compared with their healthy control group.[19] They recommended supplementation of vitamin D in management of such patients especially when co-treated with corticosteroids. Similarly, another study by Chroni et al showed that vitamin D level was abnormally low in patients with myasthenia gravis and peripheral neuropathy in Greece.[12] They also reported low levels of vitamin D even in healthy population. They proposed that low levels of vitamin D levels in healthy individuals in their country were attributed to excessive use of sun blockers to avoid sun exposure and resultant skin cancers, more indoor work during daytime and consumption of excessive amount of oil fish which reduced absorption of vitamin D in their population. Our results differ from the results of this study as our healthy patients had normal vitamin D levels which may be explained by abundant sunlight in our latitude as well as non-consumption of oil fish and negligible use of sun blockers.

Another study by Askmark et al reported deficiency of vitamin D levels in patients with myasthenia gravis in Sweden and showed improvement of fatigue in their patients after vitamin D supplementation.[20] The proposed mechanism of improved muscle activity in these patients after vitamin D supplementation was direct activation of nuclear receptors in muscle fibers of these patients which increased protein synthesis and hence increased muscle mass and performance in these patients. This poses another area of future research in which further studies can be conducted to determine the effect of vitamin D supplementation in patients with GBS. Based on previous reports on other autoimmune disease, we can anticipate betterment of symptoms of GBS after vitamin D supplementation. But recommendations can only be proposed once studies have confirmed this effect in GBS patients practically.

Another aspect to note her is statistical association of smoking with lower levels of vitamin D in GBS patients. Various studies have shown abnormally low levels of vitamin D in smokers due to downregulation of parathyroid-calcium-vitamin D axis and hence, decreased bone density in such patients[21,22]. That is the reason, GBS patients may seriously be warned to cut down on smoking as this may improve their symptoms by upregulation of their vitamin D metabolism in the body.

Our study was limited by its small sample size and not studying the effect of vitamin D supplementation on symptoms of GBS in our population. We propose future studies with large sample size and considering role of vitamin D supplementation on GBS symptoms. Another limitation of our study was exclusion of female gender from our study owing to endemically low levels of vitamin D in our population. Deficiency of vitamin D has also been reported in various other parts of the world not only in countries on northern hemisphere like North America and Central Europe but also in regions located at southern latitudes like in Turkey, Saudia Arabia and India.[23–25] Future researches should be conducted including both genders and they may reveal even higher prevalence of lower levels of vitamin D in female GBS patients in our country.

CONCLUSION

GBS occurs in male patients of Pakistan secondary to preceding respiratory or gastrointestinal infections. Vitamin D levels are significantly low in patients with GBS patients as compared to healthy normal individuals. None of the healthy male patients showed abnormally low levels of vitamin D. Smoking was significantly associated with low levels of vitamin D in GBS patients.

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COMPARISON OF EFFICACY AND HOSPITAL STAY OF MANUAL VACUUM ASPIRATION (MVA) AND UTERINE CURETTAGE IN SURGICAL MANAGEMENT OF 1ST TRIMESTER MISCARRIAGES IN JINNAH HOSPITAL LAHORE.

Shazia Sehgal, Quratulain Munir, Alia Zaineb Asad, Noreen Huma, Nudrat Sohail

Department of Gynaecology, Jinnah Hospital Lahore

Abstract

Background: Loss of pregnancy, before the fetus has become viable, is termed as miscarriage. Miscarriage not only affects the physical but also the psychological health of a woman. The first trimester miscarriage is managed conservatively, medically and surgically. The main surgical procedures of evacuation of retained products of conception are manual vacuum aspiration and evacuation followed by sharp curettage. Both these procedures have their own pros and cons and a comparison between the two can help in management decisions.

Objectives: To compare the efficacy and mean hospital stay after manual vacuum aspiration (MVA) and uterine curettage in management of first trimester miscarriage.

Study Design: Randomized control trial.

Setting: Department of Obstetrics and Gynecology, Unit-3, Jinnah Hospital, Lahore.

Study Duration: April 2017 to December 2017.

Subjects and Methods: A total of 200 patients (100 in each group) were selected for the study. In Group-A (MVA) manual vacuum aspiration was done and in group-B (UC) uterine curettage was performed.

Results: Mean age was 28.51±8.10 and 28.31±8.33 years in group-A and B, respectively. In group-A (MVA) mean hospital stay was 4.23±1.4 hours and in group-B (uterine curettage) mean hospital stay was 7.91±2.1 hours and was statistically significant. ($p<0.001$). Group-A (MVA) was more efficacious as compared to group-B (UC). ($p=0.005$).

Conclusion: Manual vacuum aspiration (MVA) for management of first trimester miscarriage is an effective procedure as compared uterine curettage, with obviating need for general anesthesia and an access to theatre. Complications rate in such as retained conception products, uterine perforation, bleeding are minimum as compare to uterine curettage.

Key Words: First trimester, Miscarriage, Manual vacuum aspiration, uterine curettage

Miscarriage is loss of intrauterine pregnancy of <24 weeks of gestation. WHO definition of miscarriages is expulsion of fetus weighing 500 grams or less[1]. Early pregnancy loss is loss of pregnancy <12 weeks of gestation.[2]

Miscarriage is very traumatic and highly emotional event for a woman and her partner and its effect is always underestimated by all those who are involved in their care. Miscarriage is a common complication of pregnancy occurring in 12-30% of all clinical pregnancies.[3]

Global data shows that many women till age of 45 years have at least one abortion in life time.[4] Local data suggest that the annual abortion rate is approximately 29/1000 in women of ages from 15 to 49 years.[5-6] Although the medical technology has advanced considerably, almost 1/3rd of abortions are performed under unsafe conditions which can lead to 13% of maternal deaths.[5,7]

The retained products of conception are removed medically, by manual vacuum aspiration or by sharp curettage. Vacuum aspiration is one of the

widely used method in terminating early pregnancy for >30 years. It is more safe and less painful than sharp curretage.[4,5] It is usually performed under local anesthesia.[9,10] Success rate of manual vacuum aspiration is almost 95-100%.[4,5]

Vacuum aspiration apparatus aspirates the uterine contents using a metallic or plastic cannula which is attached to a 60 ml syringe with a plunger which is self-locking. It produces vacuum for aspiration of retained products of conception.[4,5,9] Manual Vacuum Aspiration is performed under local anesthesia in procedure room therefore the operation theater and general anesthesia are not required.[11] This procedure can be performed in primary care settings at a lower cost and shorter hospital stay than required for sharp curettage.[4,5]

METHODS

A randomized control trial was conducted at gynecology and obstetrics unit 3, Jinnah hospital April 2017 to December 2017. Sample size of 200 (100 in each group was calculated with 95% level of significance, 80% power of study and an expected percentage of efficacy in both groups i.e. 99.3%[15] vs 89.6%[5] for dilatation and curettage and MVA respectively through a non-probability / purposive sampling technique. All patients coming to OPD and emergency between age between 15-45 years, in 1st trimester missed abortion or Incomplete abortion and USG suggestive of retained products of conception with gestational age of less than 12 weeks according to last menstrual period or USG were included in study. Patient with uterine anomalies, history of coagulation disorders, expected ectopic pregnancy assessed on USG showing no intrauterine gestational sac or ectopic pregnancy anywhere else and febrile, septic or otherwise unstable patients (fever > 100F° or TLC of >12,000) were excluded from study. First trimester was defined as gestational amenorrhea of less than 12 weeks by dates or gestational sac of > 20mm with no yolk sac or > 25mm with no visible fetus was considered missed abortion or early fetal demise and incomplete abortion. Efficacy was defined as post-treatment pelvic USG revealing no to less than 15mm size retained products of conception were considered efficacious and hospital stay of < 10 hours is short stay and if >10 hours was considered the long stay. Patients were discharged when pain free, mobile, mild to no vaginal bleeding. Subjects were evaluated by detailed history, examination, baseline investigations, pelvic USG and exclusion criteria were followed strictly. After and informed consent benefits and side effects of procedure were explained to patients. Patients were divided in to two groups by lottery method, group-A and B. Group-A was undergone MVA and group-B undergone uterine curettage. Both procedures were performed in minor operation theatre. MVA was performed under local anesthesia paracervical block with 20ml of 10% lignocaine at 5 and 11o clock positions alone or in combination with a systemic analgesia (Nalbin + Diazepam). Need for general anesthesia was determined by patient acceptability to pain. Uterine curettage was performed under general anesthesia and products of conception were sent for histopathology. Patient was kept in recovery room for 2 hours and then was sent respective ward. Efficacy of procedure was determined by no retained product of conception on USG and complications such as uterine perforation, injury to cervix or infection were observed. Hospital stay was subsequently followed according to post-operative pain and bleeding. Data was entered and analyzed on SPSS version 17. Quantitative variables were presented as mean and standard deviation and efficacy as frequency and percentage . An independent t-test was applied to all quantitative variables i.e. mean hospital stay. Chi square was applied to all qualitative variables i.e. efficacy to test hypothesis. P value of <0.05 was taken as statistical significant.

RESULTS

A total of 200 patients (100 in each group) were included in this study.

Mean age was 28.51±8.10 and 28.31±8.33 years in group-A and B, respectively. 42.0% of the patients in group A and 39.0% in Group B were between 21-30 years of age. (Table-1). In group-A (MVA), 22 patients (22.0%) and in group-B (uterine curettage), 24 patients (24.0%) were Primigravida, while 78 patients (78.0%) in group-A and 76 patients (76.0%) in group-B were multigravida (Table-2). In group-A (MVA) mean hospital stay was 4.23±1.4 hours and in group-B (uterine curettage) mean hospital stay was 7.91±2.1 hours and was statistically significant among two groups (p<0.001) (Table-3). When comparison was made between group-A (MVA) and B (uterine curettage) for efficacy, it was observed that group-A was more efficacious as compared to group-B (p=0.005) (Table-4).

DISCUSSION

Miscarriage or abortion is the loss of pregnancy in early period up to 24 weeks and is commonly experienced by parturients. First trimester miscarriage is responsible for a large number of pregnancy losses.[14] Almost one in every four women will experience a first trimester loss in her life time.[15] Local data of women 15 to 45 years of age shows that 29/ 1000 women have first trimester abortion per annum.[6] Approximately 15 % clinically recognized pregnancies end up as either incomplete or missed miscarriage.[16]

In the developing countries, unsafe abortion practices and its related complications cause 10-13% of maternal deaths.[7] There is a need to search for safe and cost effective methods to evacuate the uterus. The methods which are commonly used include expectant management, medical manage-ment using misoprostol, manual vacuum aspiration and uterine curettage. Vacuum aspiration has become popular and is a widely used method due to its safety. It is also associated with less pain than evacuation and curettage (E&C) method and use of misoprostol.[15] The success rate of manual vacuum aspiration is reported to be between 95-100% in various trials, thus making it a highly effective method of uterine evacuation.[15,16]

There are two types of vacuum aspiration apparatus, electrical vacuum aspiration (EVA) which need an electric vacuum pump while the other is known as manual vacuum aspiration (MVA) in which the vacuum is created using a hand activated plastic syringe. Manual vacuum aspirator is lighter in weight, low in cost, can be performed under local anesthesia and does not need electricity thus making it superior to EVA. It can be especially used in low resource areas of developing countries where there is lack of electricity and non-availability of surgical suites are not usually available.[16,17,18]

Table 1: Age Distribution among Groups

Age (Year)	Manual Vacuum Aspiration (Group-A)		Uterine Curettage (Group-B)	
	Frequency	Percentage	Frequency	Percentage
< 20	20	20.0	23	23.0
21-30	42	42.0	39	39.0
31-40	28	28.0	27	27.0
41-45	10	10.0	11	11.0
Total	**100**	**100.0**	**100**	**100.0**
Mean ± SD	**28.51±8.10**		**28.31±8.33**	

Table 2: Distribution of Cases by Parity

Parity	Manual Vacuum Aspiration (Group-A)		Uterine Curettage (Group-B)	
	Frequency	Percentage	Frequency	Percentage
Primigravida	22	22.0	24	24.0
Multigravida	78	78.0	76	76.0
Total	**100**	**100.0**	**100**	**100.0**

Table 3: Comparison in Terms of Hospital Stay (hours)

Hospitals stay (hrs.)	Mean	SD	t value/ P value
Manual Vacuum Aspiration (Group-A)	4.23	1.4	t=14.580 p<0.001
Uterine Curettage (Group-B)	7.91	2.1	

Table 4: Distribution of Cases by Efficacy

Efficacy	Manual Vacuum Aspiration (Group-A)		Uterine Curettage (Group-B)		Chi Square P value
	Frequency	Percentage	Frequency	Percentage	
Yes	99	99	90	90.0	**X^2=7.79**
No	01	01	10	10.0	**P**=0.005
Total	**100**	**100.0**	**100**	**100.0**	

For more than 30 years manual vacuum aspiration is being used safely and effectively for the evacuation of early pregnancy losses.[19,20]

Although MVA is simple easy to hand and a low cost procedure, its usage in most of the hospitals even in the developing countries is restricted because many clinicians are not familiar with its use. The technique of manual vacuum aspiration was introduced in our institution only recently. The technique is naive for young residents as well other faculty members who were more used to with EVA. The success rate is high alone with no major complications like heavy bleeding, uterine perforation etc. with MVA proves that this technique is safe, cost effective and easy to learn and perform.

In present study, Manual Vacuum Aspiration group was more effective than Uterine Curettage group (99% vs 90%) with p value 0.005. It has been shown that MVA is a safe and effective method of uterine evacuation[13] and has been successfully used for the management of incomplete and missed miscarriage and termination of first-trimester pregnancy.

Our study recommended that MVA has advantages over uterine curettage for reducing hospital stay (4.23±1.4 vs 7.91±2.1) p<0.001 which is comparable with the study of Blumenthal et al.[21] Another study by Farooq et al is also consistent with our findings where they showed hospital stay of 3.48±1.2 hours in MVA group as compared 7.42± 1.93 minutes in curettage group.[12] While Tasnim et al demonstrated hospital stay of 12.26±6.97 hours in MVA.[5]

Manual vacuum aspiration is thus a well-tolerated surgical option for the management of early pregnancy loss. It is also easy to perform and has potential economic benefits. Potential complications of general anesthesia are also avoided. This should ideally be corroborated in the context of randomized controlled studies comparing MVA and uterine curettage.

CONCLUSION

Manual vacuum aspiration (MVA) for management of first trimester miscarriage is an effective procedure as compared uterine curettage, with obviating need for general anesthesia and an access to theatre. Complications rate in such as retained conception products, uterine perforation, bleeding are minimum as compare to uterine curettage. It is simple procedure that can be easily performed even by young naïve residents with a comparable cost-effectiveness. It's an effective addition for women's choice among available methods and is advantageous for both the patient and the healthcare system and can be considered as an alternative option in management of early pregnancy loss.

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ATTENUATION OF SYMPATHETIC RESPONSE TO LARYNGOSCOPY AND TRACHEAL INTUBATION: INTRAVENOUS FENTANYL Vs LIGNOCAINE

Muhammad Naveed Azhar[1], Aamir Bashir[2], Sajjad Hussain[3]

[1]Registrar Anesthesia & Intensive care, University Hospital Waterford Dunmore Road, Waterford Ireland; [2]Assistant Professor Anaesthesia, Shahlamar Medical & Dental College Lahore; Pakistan; [3]Assistant Consultant Anesthesia, Dr. Suleiman AL Habib Hospital, Rayan Branch Riyadh, KSA,

Abstract

Background: Endotracheal intubation is often associated with hypertension and tachycardia primarily due to sympatho-adrenal stimulation. Many drugs like local anesthetics, opioids, calcium channel blockers, beta blockers and glyceryl trinitrates have been used to blunt this harmful response to avoid myocardial ischemia and other deleterious effects.

Objectives: To compare the efficacy of intravenous fentanyl with lignocaine to blunt the sympathetic response of laryngoscopy and tracheal intubation in patients undergoing elective surgery.

Study Design: Randomized clinical trials.

Place and duration of study: Operation theatre, Shaukat Khanum Memorial Cancer Hospital & Research Center, Lahore over a period of six months.

Material and methods: A total of 230 patients equally divided in two groups either to receive intravenous lignocaine 1.5mg/kg or fentanyl 2µg/kg. Endotracheal intubation done after routine induction of anesthesia. Prevention of rise in heart rate more than 100/min was considered as blunting of sympathetic response. Data collection done on prescribed proforma.

Results: Patients in Fentanyl group experienced less rise in heart rate (p: 0.004) as compared to lignocaine group (p: 0.514).

Conclusion: We concluded that fentanyl was better choice when compared with lignocaine to blunt the sympathetic response of laryngoscopy and tracheal intubation in patients undergoing elective surgery.

Key words: Fentanyl, Lignocaine, sympathetic response, laryngoscopy, tracheal intubation.

Tracheal intubation stimulates laryngeal and tracheal receptors, resulting in marked increase in the elaboration of sympathomimetic amines. This sympathetic stimulation result in tachycardia and a rise in blood pressure and arrythmias.[1] Many pharmacological methods have been advised to blunt this response of laryngoscopy and tracheal intubation including local anesthetics like lignocaine, opioids like fentanyl, remifentanil, tramadol, vasodilators like glyceryl trinitrates, beta blockers like esmolol and labetalol. [2]

Hussain and Zaeem concluded that Glyceryl trinitrate is more effective than plain lignocaine in blunting the hypertensive stress response of intubation.[3] Min JH et al found that remifentanil 1 mg/kg was more effective than the combination of lidocaine 1.5 mg/kg and esmolol 1 mg/kg for attenuating the hemodynamic responses to rapid sequence intubation.[4]

Different types of laryngoscopes have also been used to see the effects on cardiovascular response of laryngoscopy and tracheal intubation. Liu HP and

Correspondence: Dr. Muhammad Naveed Azhar, University Hospital Waterford Dunmore road, Waterford Ireland naveedazharskmch@gmail.com,

his colleagues did a comparison of cardiovascular responses between orotracheal and nasotracheal intubation with the aid of Glide scope video laryngoscope. Intubation in orotracheal group caused significant increases in heart rate and compared with those in nasotracheal group. [5]

Fentanyl is a synthetic opioid and acts on u-receptors. It is used frequently as an adjunct to induction agents to blunt the hemodynamic response to laryngoscopy and tracheal intubation, which can be particularly severe in patients with hypertension or cardiovascular disease. Common clinical practice involves titration of fentanyl in doses of 1.5 to 5 µg/kg prior to administration of the induction agent. Because its peak effect lags behind peak plasma concentration by 3 to 5 minutes, fentanyl titration should be complete approximately 3 minutes prior to laryngoscopy to maximally blunt hemodynamic responses to tracheal intubation.[6] Lidocaine is a common local anesthetic and antiarrhythmic drug. The efficacy profile of lidocaine as a local anesthetic is characterized by a rapid onset of action and intermediate duration of efficacy. Lidocaine alters signal conduction in neurons by blocking the fast voltage gated sodium (Na+) channels in the neuronal cell membrane that are responsible for signal propagation. With sufficient blockage the membrane of the postsynaptic neuron will not depolarize and will thus fail to transmit an action potential. This creates the anesthetic effect by not merely preventing pain signals from propagating to the brain but by stopping them before they begin. Careful titration allows for a high degree of selectivity in the blockage of sensory neurons, whereas higher concentrations will also affect other modalities of neuron signaling.[7]

There exist some controversies regarding use of lignocaine and fentanyl whether they blunt the cardiovascular response or not. Hence this study was designed to compare the effect of these two drugs; lignocaine and fentanyl, which one has a better profile to blunt the sympathetic response of laryngoscopy and tracheal intubation. The data from this study would help health care professional to use a better agent to blunt this harmful reflex of laryngoscopy and tracheal intubation.

OBJECTIVES

To compare the efficacy of intravenous fentanyl with lignocaine to blunt the sympathetic response of laryngoscopy and tracheal intubation in patients undergoing elective surgery.

Efficacy: No sympathetic response to laryngoscopy and tracheal intubation.

Sympathetic Response: Heart rate more 100 beats/minutes after the laryngoscopy and tracheal intubation is regarded as sympathetic response.

Hypothesis: Intravenous fentanyl is more effective than intravenous lignocaine in blunting the sympathetic response of laryngoscopy and tracheal intubation in patients undergoing elective surgery.

METHODS

Study Design: Randomized clinical trials.

Place and duration of study: Operation Theater, Shaukat Khanum Cancer Hospital & Research Centre, Lahore over a period of six months.

Sample Size: Sample size of 230 cases (115 in each group) calculated with 80% power of test, 1% level of significance and taking expected percentage of efficacy (in terms heart rate less than 100 beats/minutes) in both groups i.e. 45% in fentanyl group Vs 25% in lignocaine group in patients undergoing elective surgery.

Sampling Technique: Non-probability Purposive Sampling.

Sample Selection: Patients aged 18-60 years of either gender having American Society of Anesthesiologist (ASA) status I & II undergoing elective surgeries like mastectomy, total knee replacement, radical cystectomy, anterior resection, esophagectomy and transabdominal hysterectomy were included. However, patients refusing the consent, allergic to lignocaine and fentanyl, and patients with anticipated difficult airway (Malampatti class III & IV) were excluded from the study.

Data Collection Procedure:

After approval from Shaukat Khanum Cancer Hospital Ethical Committee and informed written consent, a total of 230 patients i.e. 115 patients in each group selected from elective surgery list fulfilling the inclusion criteria were enrolled. By using the lottery method, the participants were assigned to receive intravenous lignocaine 1.5 mg/kg (Group A) and intravenous fentanyl 2µg/kg (Group B). 'Person A' was assigned to give the medication, while 'Person B' monitored the heart rate. 'Person C' was there for intubation.

Standard anesthesia monitoring, pre-oxygenation with 100% oxygen. Participants were given either intravenous fentanyl or lignocaine according to assigned group. Induction of general anesthesia done with propofol and atracurium. Assisted face mask ventilation for 3 mins followed by laryngoscopy and endotracheal intubation done. Anesthesia maintained on Oxygen/N_2O and Isoflurane. Patient heart rate was monitored immediately after tracheal intubation and efficacy was labeled as per operational definition. Data collection done on attached proforma.

DATA ANALYSIS

Data were analyzed using SPSS version 10. Quantitative variables like age and heart rate were presented in the form of Mean ± S.D. Qualitative variable like gender and efficacy were presented in the form of frequency and percentages. Efficacy of the drugs was compared in both groups by using Chi square test. P value ≤ 0.05 was considered as statistically significant.

RESULTS

A total of 230 adult surgical patients participated in this study, 115 received lignocaine (group A) and 115 received fentanyl (group B). The two groups were comparable with respect to age (Table I) and weight of the patient (Table 2). The mean age (in years) in fentanyl group was 50.18 ± 13.75 SD as compared to lignocaine group with mean age of 48.05 ± 13.65 SD. The mean weight (in Kg) of patients in fentanyl group was 67.40 ± 5.75 standard deviation as compared to lignocaine group of which it was 66.59 ± 6.27 standard deviation. The blunting of sympathetic response of laryngoscopy and tracheal intubation by preventing the rise in heart rate more than 100 beats/min after laryngoscopy and tracheal intubation was significantly better in fentanyl group (p value: 0.004) as compared to lignocaine group (p value 0.514).

Table 1: *Age of the Patients*

Group	N	Mean age (Years)	Standard Deviation	P value
Fentanyl	115	50.18	13.75	0.000
Lignocaine	115	48.05	13.65	0.000

Table 2: *Weight of the Patients*

Group	N	Mean Weight (Kg)	Standard Deviation	P Value
Fentanyl	115	67.40	5.75	0.000
Lignocaine	115	66.59	6.27	0.000

Table 3: *Blunting of Response*

Group	Blunting of response	Frequency	Percentage	P Value
Fentanyl	Yes	73	63.5%	0.004
	No	42	36.5%	
Lignocaine	Yes	61	53.0%	0.514
	No	54	47.0%	

DISCUSSION

General Anesthesia has almost become synonyms with endotracheal anesthesia. As a matter of fact, rapid studies made in the specialty of anesthesia can directly be attributed to our ability to our ability to manage air way.

Laryngoscopy and endotracheal intubation are considered as the most critical event during general anesthesia. They provoke a transient but marked sympathetic and sympathoadrenal response manifesting as hypertension and tachycardia. These responses are unpredictable and variable; may result in potentially deleterious effects like left ventricular failure, pulmonary edema, myocardial ischemia, ventricular arrhythmias and cerebral hemorrhage.

These are by far the most important indications to blunt the hemodynamic response of laryngoscopy and tracheal intubation.[8]

Many pharmacological agents, different intubating devices and mode of intubation has been studied so far. Among the pharmacological agents used for blunting the hemodynamic response, opioids were found to be effective.[9] Singh and colleagues compared esmolol with labetalol and they expressed that labetalol in limited dose was more effective than esmolol to blunt the response of laryngoscopy.[10] Wang and colleagues used different doses of esmolol to blunt this response, and they concluded that esmolol in a dose of 1.5mg/kg not only suppress this reflex but also had no side effects.[11] Hussain and Zaeem compared glyceryl trinitrates with lignocaine to blunt the hypertensive response of laryngoscopy. Glyceryl trinitrates was more effective than lignocaine as per their results[(3)]. Hussain and Sultan compared the efficacy of fentanyl and esmolol in preventing the hemodynamic response to laryngoscopy and endotracheal intubation. They concluded that esmolol was more consistent to prevent laryngoscopy response as compared to fentanyl.[12] Yong et al also concluded that fentanyl 2µg/kg intravenous bolus was not much effective to suppress the cardiovascular intubation response in children.[13]

Ali and Mushtaq in their study concluded that intravenous lignocaine in a dose of 1.5mg/kg starting 3 minutes before laryngoscopy and intubation did not suppress significantly, the increase in heart rate and mean arterial pressure.[14] The results of our study are comparable to a trial done by Feng and his colleagues on comparison of lidocaine, fentanyl and esmolol. They concluded that the rise in heart rate more than 100 beats/minutes after laryngoscopy and intubation was 15 of 20 (75%) patients in lidocaine group as compared to 11 of 20 (55%) of patients in fentanyl group.[15]

In view of contradictory results of these studies, the present study was carried out to evaluate the effectiveness of these two drugs; fentanyl and lignocaine to blunt the sympathetic response of laryngoscopy and tracheal intubation. Our hypothesis was that the intravenous fentanyl was more effective than intravenous lignocaine in blunting the sympathetic response of laryngoscopy and tracheal intubation in patients undergoing elective surgery. Our study showed that both drugs helped in blunting the sympathetic response of laryngoscopy and tracheal intubation. However, fentanyl was effective in 73 out of 115 patients (P value 0.004) and lignocaine was effective in 61 out of 115 patients (P value 0.514). The results of our study fully supported the hypothesis that intravenous fentanyl was more effective in blunting the sympathetic response of laryngoscopy and tracheal intubation.

In summary, the results of our study were comparable with other studies used opioids to blunt the sympathetic response of laryngoscopy and tracheal intubation, however more research work is required on this topic in future.

CONCLUSION

We concluded that fentanyl was better choice when compared with lignocaine to blunt the sympathetic response of laryngoscopy and tracheal intubation in patients undergoing elective surgery.

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PREDICTIVE VALUE OF VARICELLA INFECTION IN HEALTHCARE WORKERS: A SEROPREVALENCE STUDY

Mateen Izhar[1], Saira Moeed[2], Kokab Jabeen[3], Hira Ghaffar[4], Mariya Farooq[5], Namra Younus[6]

Abstract

Introduction: Varicella zoster virus (VZV) is a member of the herpes family. It is highly contagious and spread from person to person through respiratory droplets or direct contact with vesicle fluid.. After Varicella infection, more than 95% of people develop antibodies against Varicella. These antibodies (VZV IgG) indicate lifelong immunity to Varicella.

Objectives: To determine the relationship between recall history and serological immunity against VZV amongst HCWs

Methods: 200 HCWs were investigated for immunity to VZV, employed in Shaikh Zayed Hospital in various job categories. All HCWs completed a questionnaire which elucidated previous history of Varicella history of Varicella in family members, antibody testing against Varicella and Varicella vaccination. The presence of VZV antibodies was investigated with the enzyme-linked immunosorbent assay IgG.

Results: Out of 200 HCWs tested for VZV IgG, 174 (87%) were seropositive and 26 (13%) were seronegative, indicating susceptibility to VZV infection. A previous history of chickenpox was reported by 74 HCWs, all of them were seropositive on ELISA. A negative recall was reported by 126 HCWs, out of which 100 were seropositive and 26 were seronegative on ELISA. Sensitivity, specificity, positive and negative predictive values of a self-reported history of Varicella infection were 43%, 100%, 100% and 20% respectively.

Conclusion: Positive history of Varicella was a reliable indicator of immunity among HCWs, whereas negative history was not a good predictor of immunity. VZV screening of HCWs without a history of chickenpox, and vaccination of susceptible HCWs should be mandatory, so preventing transmission of VZV to their colleagues or patients.

Varicella-zoster virus (VZV) is a ubiquitous human alphaherpesvirus. It causes two distinct exanthematous diseases: varicella and herpes zoster. Varicella or chickenpox is caused by primary infection with VZV whereas zoster or shingles occurs as a result of reactivation of latent virus. Steiner in 1875 for the first time demonstrated that chickenpox was caused by an infectious agent. He inoculated volunteers with the vesicular fluid from a patient with chicken[(1)]. Von Bokay in 1888, determined the relationship between clinical observations of varicella and herpes zoster.

The susceptible HCWs to VZV are those at risk of developing infection as no antibodies to VZV are present. In hospital settings, varicella is an occupational hazard for HCWs. Varicella may be introduced into the hospital settings through the infected patients, hospital staff or visitors. HCWs should be screened for VZV immunity at the time of employment in hospital.

In 2011, a study showed that VZV seroprevalence among HCWs in Taiwan was 91.1%[(45)]. In 2008 the VZV seroprevalence among HCWs in Kuala Lumpur, Malaysia was reported to be 84%[(46)]. In 2007, VZV prevalence was 86% among hospital staff of Riyadh[(47)]. Several studies have reported that 78% of United States HCWs have had varicella [(48)]. In 2006, Chodick reported 94.8% VZV seroprevalence among Israeli HCWs[(49)]. The published data on the epidemiology of VZV in Pakistan is very scarce[(50)]. The seroprevalence rate of VZV in Pakistan is 39.6% among males and 45.2% among females[(51)]. Celikbas in a study conducted in 2006 reported that 98% of HCWs working in Turkey had antibodies to VZV[(52)]. In 2002 Fedeli reported 97.9% VZV seroprevalence

among HCWs working in Italy.[53] The varicella susceptibility rate among HCW in Ireland is 4% and in Belgium is 1.5%.Hatakeyama reported that VZV susceptibility rate among HCWs of Tokyo hospital is 2.8%.[54]

A reasonable amount of high-quality research was found to determine the reliability of a history of chickenpox, for predicting the likelihood of immunity. Below are summarized the key findings about varicella history in HCWs:

- A history of varicella has a high positive predictive value (95–98%) in HCWs from temperate climates. In this group, history alone is sufficient to determine immunity to varicella[59] Those HCWs with a negative or uncertain history should be serologically tested.[60]
- A history of varicella has a lower positive predictive value in HCWs from tropical or subtropical climates. This group should have serological screening regardless of a history of chickenpox.[61] The variations in epidemiology of VZV among tropical and temperate coutries are due to differences in temperature and humidity which affect virus transmission.
- All the HCWs diagnosed with chickenpox should be excluded from the workplace until there are no new lesions and all lesions present have crusted over.[62]
- Susceptible HCWs who have a significant exposure to VZV should be excluded from contact with high-risk patients.
- Pregnant HCWs exposed to chickenpox should be assessed for varicella zoster immunoglobulin (VZIG).[63]
- Where HCWs have a contraindication to vaccination, eg they are immunocompromised, the risk of varicella infection to the HCW and the risk of onward transmission of infection to their patients should be assessed.[64]

Objectives

1) To determine the relationship between recall history and serological immunity against Varicella zoster virus amongst HCWs.
2) To assess the seroprevalence of IgG antibodies against VZV amongst HCWs.
3) To assess the reliability of recall Varicella history as a predictor of immunity.

Study Design:

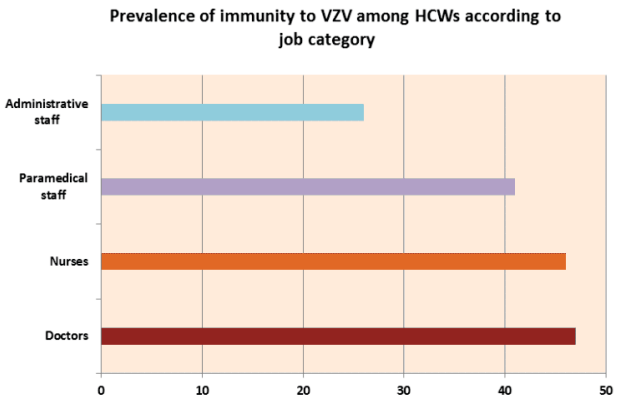
This study was a cross-sectional review of prospectively collected samples from March 2013 to February 2014 from the HCWs employed at the Federal Post Graduate Medical Institute, Shaikh Zayed Hospital Lahore, Pakistan. The samples were analyzed at the microbiology laboratory of the Federal Post Graduate Medical Institute, Shaikh Zayed Hospital Lahore, Pakistan.

Study Setting:

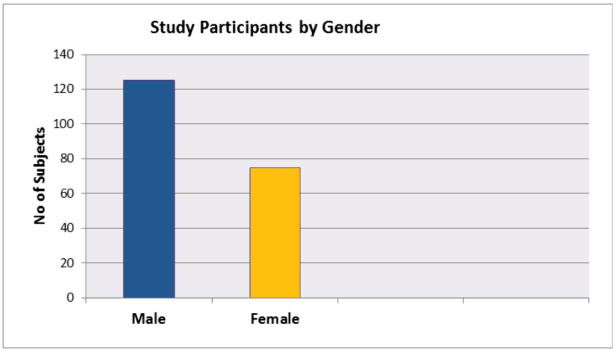
This study is based on the data collected from the Federal Post Graduate Medical Institute, Shaikh Zayed Hospital Lahore. 200 HCW's were selected randomly from all the departments. They were classified as doctors, nurses, paramedical staff and administrative staff (including maintenance, technical etc.). 50 HCW's were selected from each group.

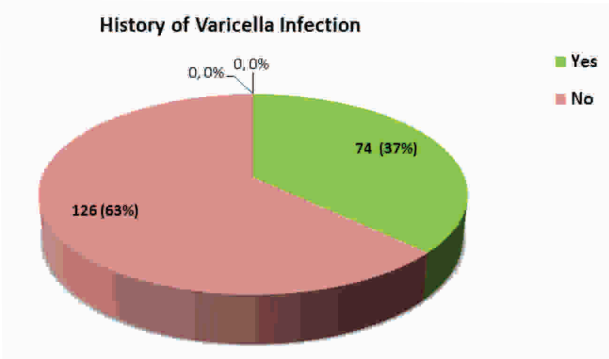
RESULTS

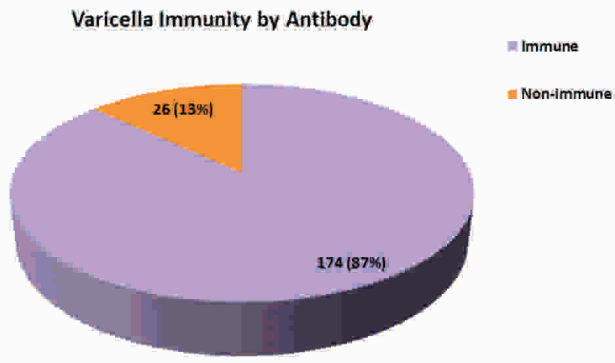
Out of 200 HCWs tested for VZV IgG, 174 (87%) were seropositive and 26 (13%) were seronegative, indicating susceptibility to VZV infection. A previous history of chickenpox was reported by 74 HCWs, all of them were seropositive on ELISA. A negative recall was reported by 126 HCWs, out of which 100 were seropositive and 26 were seronegative on ELISA. Sensitivity, specificity, positive and negative predictive values of a self-reported history of Varicella infection were 43%, 100%, 100% and 20% respectively.

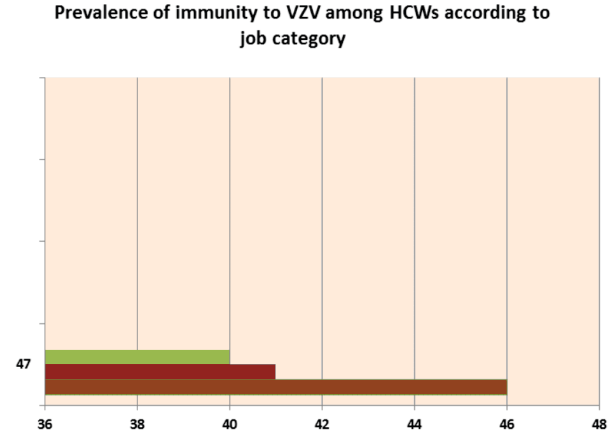


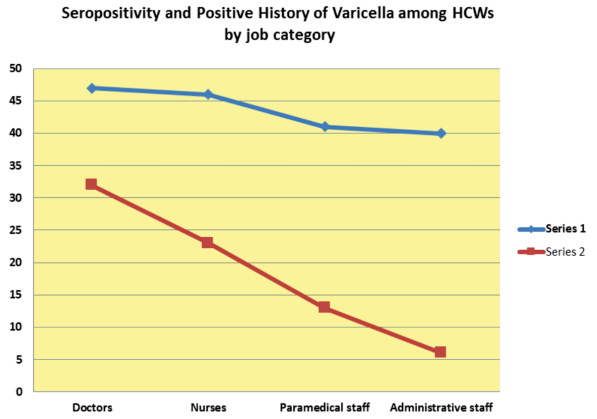
In the study, the participants were predominantly male (63%). Figure 2 displays the study participants by gender with 125 being males and 75 being females. The male to female ratio was 1.6:1.











DISCUSSION

VZV is an occupational hazard for susceptible HCWs. Varicella is a nosocomial infection among HCWs, once infected may transmit the infection to their co-workers and patients under care.[7] In this study we found that VZV susceptibility rate is 13% among HCWs of Shaikh Zayed hospital, a tertiary care hospital in Lahore. This susceptibility rate is higher than western countries. The VZV susceptibility rate among HCWs in USA was 1-5%, in Ireland was 4% and in Belgium was 1.5%. Hatakeyama et al (2004) reported that VZV susceptibility rate was 2.8% among HCWs of Tokyo hospital.[4]

In the present study, it was found that VZV seropositivity was 87% among HCWs of this hospital. Only 37% (74 out of 200) HCWs reported a positive history of varicella. However, varicella immunity was documented in 100% of HCWs (74 out of 74), who reported a positive recall history of varicella. Therefore, positive history of varicella was an excellent predictor of VZV seroprevalence among HCWs[(8)]. Sensitivity, specificity, positive predictive value and negative predictive value of recall history of varicella to predict the varicella immunity were 43%, 100%, 100% and 20% respectively. When immunity levels are above 94%, then viral transmission got interrupted in the hospital setting. The VZV seropositivity level is not so high in this hospital to prevent future outbreaks of varicella, so necessary interventions to prevent VZV transmission should be under taken.

Celikbas et al (2006) from Turkey investigated

363 HCWs and reported that VZV seroprevalence was 98%.[2] Almuneef et al (2006) studied 4006 new HCW recruits in Saudi Arabia and found that VZV seroprevalence was 86% (68). In Taiwan (2012), prevalence of VZV seropositivity was reported to be 91% among HCWs. Sam et al (2008) from Kuala Lumpur found that 82% of the HCWs were seropositive in Malaysia.[14] MacMahon et al (2004) in UK reported seroprevalence of VZV was 91.7% among HCWs.[12]

Most of the HCWs range between 18-32 years of age in this study. Our data showed that 98% HCWs who reported positive history of varicella, contracted it at the age between 5-10 years.

Some studies examining HCWs recommend serological testing of all the HCWs, regardless of their past varicella history. Their authors suggest that VZV screening of all HCWs, decrease the chance of missing any susceptible employee.[6,7] In contrary, there are several studies advocating the selective serological testing of HCWs, only with a negative history of varicella.[7,10] They emphasize on the reliability of self-reported varicella history as a predictor of VZV seroprevalence.

In 2007, Apisarnthanaraket al determined the relationship between immune status and history of varicella among HCWs.[4] The study was conducted on 110 HCWs in Thailand. He reported a PPV of 100% and a NPV of 61%.This study shows that self-reported history of varicella was a good predictor of immunity. A positive history of varicella correlates well with the seroprevalence of VZV, whereas a negative history of varicella was not a reliable predictor of immunity.

Santos et al (2004) conducted a study on 215 HCWs in neonatal units in Sao Paulo University hospitals. 100% of the HCWs who reported a positive history of varicella were seropositive for VZV and 92% of the HCWs with a negative history were also found immune to VZV on ELISA.[10] Kanra et al (2003) compared history of varicella versus serological testing for VZV prevalence among medical students[(11)]. He reported that history of varicella to detect VZV seroprevalence had a good PPV and poor NPV.

Holmes (2005) suggested that positive history of varicella was reliable, but a negative history was not. Most studies concluded that serological screening of the HCWs with a negative history was advisable, prior to VZV vaccination.[12] Waclawski and Stewart (2002) in Scotland examined susceptibility to VZV among applicants for nurse training. 356 nursing applicants submitted a questionnaire and serological screening was done by ELISA which detect VZV IgG antibody.[14] They found that PPV of a history of varicella for the seropositivity was 98% and the negative predictive value was 14%. They concluded that a positive history of varicella was a reliable predictor of immunity whereas negative history was an unreliable identifier of susceptibility to VZV in HCWs. Serological screening of all HCWs was advocated, because selective screening using past history alone would have missed 40% of the susceptible HCWs to VZV.

In the present study, more than half of the HCWs (100 out of 126) with a negative history of varicella were found seropositive for VZV (79%). Only 20% were found seronegative, so susceptible to VZV infection. It means negative history of varicella did not predict lack of immunity. Therefore HCWs with negative history of varicella should be serologically tested, prior to VZV vaccination, because a major proportion of those HCWs would be serologically immune to VZV.

Interestingly, majority of HCWs (135 out of 141) with a positive history of varicella among family members were seropositive for VZV. 95% HCWs with a positive history of varicella among family members were found immune to VZV. This may be because history of varicella among family members causes prior exposure of HCWs to VZV, resulting in development of immunity against VZV. The exposure to VZV causes development of life-long immunity.

In this study, no significant difference found in terms of VZV seroprevalence between male and female HCWs. However, the association between job category and seroprevalence of VZV was

highlighted. The prevalence of seronegativity was significantly less in doctors than other medical professionals. The recall history of medical professionals (doctors, nurses & paramedical staff) was more significantly valid, than of administrative staff. This may be because medical professionals have enhanced knowledge of varicella as compared to the administrative staff. Sensitivity was significantly higher for doctors (68.1%) than nurses (51%), paramedical staff (31.7%) or administrative staff (15%). Similarly a study in Taiwan (2012), has reported that sensitivity and PPV for the recall history of varicella were significantly higher in doctors than other medical professionals[15]. Doctors and nurses had higher seropositivity rates than other HCWs.

This study suggests that it would be more cost effective to serologically test only HCWs with a negative history, before varicella vaccination. This research work is based on samples from only one tertiary care hospital in Lahore. So the results may not be generalized to HCWs working in other hospitals around Pakistan. Further extensive researches covering HCWs working in other hospitals of Lahore is the need of hour. This work can be used as a guideline in the formation of varicella vaccination program in this hospital, which is the need of the hour.

CONCLUSION

Positive history of Varicella was a reliable indicator of immunity among HCWs, whereas negative history was not a good predictor of immunity. VZV screening of HCWs without a history of chickenpox, and vaccination of susceptible HCWs should be mandatory, so preventing transmission of VZV to their colleagues or patients.

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SURGICAL MANAGEMENT OF ASPERGILLOMA - A REVIEW OF 30 CASES

Ghulam Shabbir Pervez, Saqib Raza Bukhari, Saima Sultan, Ahsen Nazir Ahmad, Mohsin Geelani, Muhammad Afzal, Faiza Siddique, Obaid ur Rehman, Ahmad Abutalib

Department of Thoracic Surgery, Gulab Devi Chest Hospital & Sharif Medical and Dental College, Lahore

Abstract

Introduction: Superadded infection in cavitary lesions particularly in compromised patients is very common. It occurs as aspergilloma or fungal ball and usually presents as frank recurrent haemoptysis .The medical treatment is usually not effective and surgery is the treatment of choice. Unfortunately most patients are not good candidates so one has to adopt different surgical techniques.

Material & methods: There were 30 patients who underwent pulmonary surgery for symptomatic aspergilloma from January 2008 to December 2009, 14 female and 16 male, with a mean age of 30 years (range 21–50 years). The most common manifestations were, haemoptysis in 24(80%) and recurrent infections with undiagnosed suspicious lesions in 10(33%). The mean duration of the symptoms was 5 years (range 1–25 years). History of previous lung disease was present in 26 patients (86%). A lobectomy was performed in 18 patients (60%), segmental / wedge resection in 8(27%) and evacuation of fungal ball with obliteration of cavity in 4(13%). Results: There was no post-operative death and a few complications occurred in 6(20%) cases. Major complications included were bronchopleural fistula 4(13.3%) and hemorrhage 2(6.6%). Complication occurred in 5/12 cases of segmental resection / cavernostomy (evacuation of fungal ball and obliteration of cavity) while only 1/18 case of lobectomy had bronchopleural fistula. Conclusions: Surgery offers definitive and long term symptom-free survival in cases of pulmonary aspergilloma at a negligible risk; though almost one-fourth of those undergoing surgery develop some complications, these are largely manageable. They are due to incomplete resection as shown by increased number of complications in this group as compared to lobectomy.

Key words: Aspergilloma, Cavitary lesion, fungal ball, Lobectomy.

An aspergilloma, also known as a mycetoma or fungus ball, is a clump of fungus which exists in a body cavity such as the lung. It is associated with the Aspergillus species[1] most often. Inadequate drainage is thought to facilitate the growth of Aspergillus on the walls of these cavities. Aspergillus is a common fungus. A. fumigatus is commonest species but other fungi may also cause the formation of a fungal ball, such as zygomycetes and fusarium. Aspergillus species are ubiquitous fungi acquired by inhalation of airborne spores and may cause life-threatening infections especially in immuno-compromised hosts[2]. They are commonly isolated from the soil, plant debris, and the indoor environment, including hospitals. Characteristically, the aspergilloma (fungus ball) is composed of fungal hyphae, inflammatory cells, fibrin, mucus, and tissue debris. It most commonly affects lung but can also affect brain, kidney and Para-nasal sinuses. The disease usually presents with the symptoms of cough, haemoptysis (seen in up to 75% of patients), and chest pain, shortness of breath, wheezing, weight loss and fever. Many cavitary lung diseases are complicated by aspergilloma, including tuberculosis, sarcoidosis, bronchiectasis, bronchial cysts and bulla, ankylosing spondylitis, neoplasm, and pulmonary infection[3, 4]. Of these, tuberculosis is the most common associated condition[5]. The fungus ball may move within the cavity, but does not usually invade the surrounding lung parenchyma or blood vessels, although exceptions have been noted[6,7]. The mortality rate from haemoptysis related to asper-

gilloma ranges between 2% and 14%. The surgical therapy is the most favored treatment as antifungal drugs usually fail to manage the situation.[8] The surgery in these cases is unfortunately associated with great morbidity and mortality. Large no of these patients are suffering from co morbid pathology that makes surgery difficult in these patients. A surgical resection can save these patients from recurrent frank haemoptysis and recurrent chest infections. However the basic principle of maximum healthy lung saving prevails. In spite of the risks associated with surgical treatment, resection for Aspergiloma is documented as old as 1948.[8] Arterial embolization in current scenario is considered for patients who cannot undergo surgery but surgery is still the curative treatment.[9] Surgery assures cessation of symptoms like haemoptysis and infection thus increasing the life span and improving quality of life. Surgery has been recommended even as a prophylactic treatment by some authors.[10] Presented study reviews our experience regarding indications and outcome of surgery in patients who were operated for Pulmonary Aspergiloma in our department.

METHODS

During a course of 2 years we operated upon 30 patients who were admitted for various complaints and ultimately diagnosed as Aspergiloma. Some of them were diagnosed as Aspergiloma on the basis of various investigations while a few had a lesion suspicious for Aspergiloma but no clear cut diagnosis achieved prior to surgery. All the patients were investigated by standard investigations including chest x-ray, CT Scan Thorax and Fiber optic bronchoscopy. All these patients opted for a surgical management and were declared fit for surgery and anesthesia. Their clinical presentation, investigations and surgical procedure performed were recorded. The complications and follow up were also recorded and tabulated.

RESULTS

Most of these patients belonged to productive age group i.e. 21- 50 years. Males were slightly more in number. Haemoptysis was the most commonly encountered presenting complaint. A recurrent chest infection for more than 5 years along with a suspicious lesion on chest x-ray was the other common complaint at presentation. There was a history of cough and fever in all the patients while 25 of them were diabetics. A history of previous chest disease was present in 26 patients. Anti TB chemotherapy had been given to all these patients at different times by various physicians. However all were smear negative for TB at the time of surgery. They were subjected to various investigations for the purpose of diagnosis and surgical fitness. After the initial workup, all these patients were operated and any of the following three procedures was performed.

Lobectomy (Resection of one or two lobes)

Segmentectomy or wedge resection

Cavernostomy

The preference was given to save the maximum viable lung tissue and resecting the lesion in Toto. Lobectomy for one or two lobes of lung was performed where the lesion was extensive involving a lobe of the lung and patient tolerated the procedure perop. A Segmentectomy or wedge resection was performed in those cases that had a limited focal lung involvement of the disease. In the patients who had a badly adherent lung, extensive lesion, or did not tolerate lung resection, the fungal cavity was opened after securing the chest cage and fungal material evacuated after which the space was occluded with an intercostal muscle flap. This method, however, was performed in a limited number of patients who had high per-operative risk for pulmonary resection.

The results were tabulated and tables shown hereafter are the results that were actually found.

Table 1: *Age & Sex n=30*

Age in Years	No. of patients	%
20-30	8	26.7
30 – 40	15	50
40 - 50	7	23.3
Sex		
Male	16	53.3
Female	14	46.7

Table 2: Presenting Complaints & Duration n= 30

Symptom	No. of patients	%
Cough	30	100
Fever	30	100
Chest pain	12	40
Recurrent chest infections with Suspicious lesion on X-ray Chest	10	33.3
Shortness of breath	16	53.3
Haemoptysis	24	80
Duration < 5 years	10	33.3
Duration > 5 years	20	66.7

Table 3: Basis of Diagnosis n=30

Diagnosed on	No. of patients	%
Symptoms & Radiology	20	66.7
Bronchoscopy and Lavage	6	20
Not confirmed diagnosis	4	13.3

Table 4: Procedure Performed n=30

Procedure	No. of patients	%
Lobectomy	18	60
Segmental/ wedge resection	8	26.7
Cavernostomy	4	13.3

Table 5: Complications n=30

Complication	No. of patients	%
Broncho-pleural fistula	4	13.3
Haemorrage	2	6.6

DISCUSSION

Aspergiloma is a quite common complication observed particularly in chest patients. Any cavitary lesion can attain a superadded infection that ultimately turns to form a fungal ball or Aspergiloma. The greater number of these patients belong to Asia and Africa as observed by Ashok Muniappan et al[11] Classically the condition has been divided in two groups simple and complex on the basis of radiological appearance. The management has been challenging in the past years as majority of these patients are not good candidates due to compromised lung. Surgery assures the definite management but has greater risk element due to the poor lung status of these patients.. Cough and Haemoptysis are by far the most significant presenting symptoms observed by most of the workers and that stands right in our study also[8,11]. We did not divide these patients in to simple and complex groups because the alarming feature of haemoptysis demanded an urgent surgical intervention regardless of this distribution. The basis for diagnosis as described in different studies is symptomtology and radiological evidence. We diagnosed these patients on the same basis but in addition, some of our patients were also diagnosed on the basis of histopath (13.3%). These patients presented with a complaint of haemoptysis but a definite diagnosis was not achieved until they were subjected to surgery and the resected tissue sent for histopathological analysis. As a matter of protocol, every patient admitted with complaint of haemoptysis in our setup, has to undergo a bronchoscopy and the lavage taken is submitted for various tests including fungal stain also. 20 % of our patients had a fungal culture positive. Different manures have been tried while operating upon these patients. We followed Akbari et al[8] in selection of surgical procedure. Maximum patients were offered removal of a complete lobe (60%). However, following the standard surgical principle of saving maximum viable lung tissue, a Segmentectomy or wedge resection was performed wherever possible. Patients who could not afford a resection due to technical reasons were offered Cavernostomy. In these patients (13.3%) the cavity was opened and a marsupalization along with an intercostal muscle flap was done after evacuating fungal material. The management offered to these patients was in accordance with Kim et al.[12] Some of these patients had a densely adherent lung to the chest wall which gave extraordinary bleeding. Therefore the option of Cavernostomy was used in these patients. Various studies have determined different complication rate from 26% to 30 %.[8,11] We had a complication rate nearly 13% with no mortality. This could be attributed to our limited Cavernostomies which usually end up in numerous complications. All of our patients who underwent a total resection remained complication free. In the rest, however, complications like

bronchopleural fistula or excessive hemorrhage were encountered but they were successfully managed. Only 2 patients had to be re-opened for securing haemostasis and it was successfully done within 24 hours of surgery. A routine follow-up on monthly intervals was made up to one year and no serious complication observed in all these patients which indicates a fair enough recovery.

CONCLUSION

We conclude that surgery for Aspergiloma is strongly recommended as it has got a very small risk factor associated with a complete cure of the ailment. The preference should be given to total resection which has negligible risk. It is also recommended that the principle of conserving maximum viable lung tissue should be followed in surgical management and Cavernostomy can be done in the patients where no other option is left to save the patient`s life from threat of haemoptysis.

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OUTCOME OF IMMEDIATE POSTPARTUM INTRAUTERINE CONTRACEPTIVE DEVICE INSERTION IN VAGINAL DELIVERY VS INCAESAREAN: A COMPARATIVE STUDY

Iram Inam[1], Shazia Sehgal[2], Sadia Sarwar[3]

[1]Associate Professor Continental Medical College, Lahore; [2]Assistant Professor AIMC, Lahore; [3]Assistant Professor Continental Medical College, Lahore

Abstract

Background: Contraception remains a major issue especially in developing countries like Pakistan. Intrauterine IUCD insertion after vaginal delivery remains a safe, reliable and effective way of birth control postpartum but its efficacy after cesarean section hasn't been studied and compared with vaginal route in our population.

Objective: To look for the outcome of IUCD insertion in caesarean vs vaginal delivery in terms of efficacy and side effects.

Material & Methods: Study Design: Quasi experimental **Setting:** Gynecology unit, Ch. Rehmat Ali Memorial Hospital, Lahore. **Duration:** The study was conducted for the period of six months from May 2017 to Nov 2017. **Data Collection:** a total of 150 patients were enrolled in the study after an informed consent. PPIUCD was inserted in a proper SOP Postpartum after the delivery in both vaginal and cesarean types and then the patients were called upon on follow at 6weeks and 6 months and a preformed proforma was filled. The data was entered and analyzed in SPSS version 20.

Results: The mean age of the patients was 27.4 ± 3-8 years with 72% belonging to rural areas and only 28% coming from urban areas. Both the short term and long term complications were very less and acceptable except for missing sting which was higher in caesarian group vs vaginal group (40% vs 28%) (P value = 0.12)

Conclusion: It can be concluded from the study that immediate post-partum insertion of IUD is a safe and effective method of contraception in both caesarian as well as vaginal delivery.

Key words: Intrauterine, IUCD, Contraception, Postpartum

Most women do not desire a pregnancy immediately after a delivery but are unclear about contraceptive usage in postpartum period. There are several studies showing adverse maternal and perinatal outcomes secondary to multiple pregnancies that have less space in between. In a recent study of postpartum unintended pregnancies 86% resulted from nonuse of contraception and 88% ended in induced abortions[1] of the estimated 210 million pregnancies that occur throughout the world each year, about 38% are unintended[2]. The reported prevalence of unintended pregnancies in Pakistan is between 16-46% 03–06. Moreover these early pregnancies have worse outcomes on mother as well as child.

61% of births in subcontinent occur at intervals shorter than the recommended birth-to- birth interval of 36 months. The study shows that 65% of women in the first year postpartum have an unmet need for family planning. Postpartum period is a highly vulnerable period for unintended pregnancy as there are limited contraceptive options because mother is breast feeding the child. In Pakistan, as in many other countries, postpartum family planning is usually initiated after 6 weeks postpartum. Moreover those females who are not breast feeding their children, return of ovulation is highly unpredictable. So immediate postpartum is the best time to begin

Correspondence: Dr Iram Inam, ahnmalik@hotmail.com

contraception as women is strongly motivated at this time.

An intrauterine contraceptive device (IUCD) has many advantages for use in postpartum period as it is an effective, long term reversible contraception, is coitus independent, and does not interfere with breast feeding.[7,8] The IUCD used is Copper T 380 A, same as that for interval insertion which has proven its safety.

The main limitation in the early years of its introduction was the increased risk of spontaneous expulsion. The rates varied widely from 10 to 14%.[9–12] Meticulous attention to the correct insertion technique has significantly lowered the rate of expulsion in later years. More studies are needed to address the misconceptions and negative attitudes which are still an issue at the community level. This study is conducted in our center to analyze the safety and efficacy of PPIUCD inserted at cesarean and vaginal delivery and thereby improve the client satisfaction and continuation rates.

METHODS

This study is conducted in Ch. Rehmat Ali hospital, Lahore. After ethical board approval, antenatal counselling, 150 patients who were willing to participate in the study, were enrolled. Written informed consent was taken.

INCLUSION CRITERIA:

1. 20-35 years old
2. Delivering by caesarean and vaginal.
3. No infections
4. No postpartum hemorrhage
5. Hb. >9g%.

EXCLUSION CRITERIA:

1. Fever
2. STDs
3. Ruptured membranes for more than 24 hours before delivery.
4. Uterine abnormalities.
5. Manual removal of placenta.
6. Unresolved postpartum hemorrhage.

Vaginal or caesarean insertion of PPIUCD was done depending on their mode of delivery. In vaginal delivery, after the delivery of placenta a special inserter was used to put IUCD in through the opening of cervix and device is unloaded carefully at the fundus followed by removal of inserter and cutting of thread. In Caesarian section, by simply placing the device at the fundus of the uterus and thread is passed through the cervical Os.

Outcome measures were analyzed at follow up visits scheduled at 6 weeks and 6 months after insertion. The findings were filled in a prefilled proforma. The data was analyzed in SPSS version 20. The quantitative variables were presented in form of mean & standard deviation. Qualitative variables like age, social status, short & long term complications were represented as frequency and percentage. The results were obtained by applying CHI square test showing P value of 0.12.

RESULTS

In our study the mean age of the patients was 27.4 ± 3-8 years. The main chunk of the patient was from rural areas (72%) as compared to urban area (28%).There were 48 (32%) females who belonged to low socioeconomic status while 90 (60%) belonged to middle class family and 12 (08%) belonged to high socioeconomic status. There were 123 (82%) Muslims patients and 27 (18%) Christian patients. Table 1.

Table 1: Demographic Distribution of Study Population

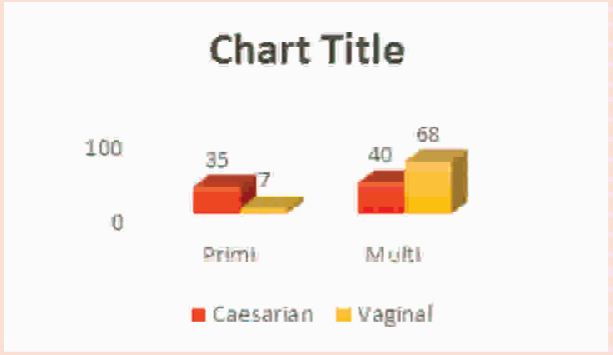
Age	Frequency	%
20-25	67	45%
26-30	46	30%
31-35	37	25%
Socioeconomic Status		
Lower	48	32%
Middle	90	60%
High	12	08%
Residence		
Rural	108	72%
Urban	42	28%
Religion		
Islam	123	82%
Christian	27	18%

In our study the ratio of prim gravida (28%) was less as compared to multi (78%) coz they were more inclined towards contraception. 85 (57%) patients were enrolled at term and 65 (43%) entered the study r at the early stage of labour. Table 2

Table 2: Obstetrical Profile of Acceptors:

Parity	Frequency	%
Primi	42	28
Multi	108	72
Gestational age		
Term	127	85
Pre-term	23	15
Time of counselling		
Antenatal	85	57
Early labour	65	43

Table 3: *Comparison of parity & route of administration:*



There were more incidences of failed induction, transverse lie, failure to progress and breech presentation which led to more cases of caesarians than normal deliveries in primis. Table 3.

Table 4: Complications at Follow up

Complications	NO	%
Short term		
Fever	1	0.6%
Discharge	1	0.6%
Expulsion	3	2%
Missing string	18	12%
Long term		
Menstrual irregularities	12	6%
Menorrhgia	10	6.6%
Discharge	3	2%
Missing string	33	22%

The incidenc of short term compications like fever (0.6%), discharge (0.6%), expulsion (2%) was negligible. The long term complication like mennorhagia (6.6%), menstrual irregularities (6%), long term discharge only 2% were also very low except for missing strings which in the short term was 12% and long term 22% having a and more via caesarian route P value 0.12.Table 04 & 05

Table 5: Comparison of Missing Strings & Route of administration

Mode of Insertion	Missing String				Total
	Yes		No		
	No.	%	No.	%	
Vaginal	21	28%	54	72%	75
Caesarian	30	40%	45	60%	75
Total	51	34%	99	66%	150
***P-value = 0.12**					

DISCUSSION

Postpartum insertions neither increase the risk of infection, bleeding, uterine perforation or endometritis, nor do they affect the return of the uterus to its normal size.[13]

The study showed that maternal age is an important factor in contraceptive acceptance. A study by Usha Ram et al have shown that the unmet need for family planning is alarmingly high among those aged 20-24 years (15%) for spacing and over 6% for limiting method.[14] In a study published by a teaching institution in Nigeria showed the model age group of clients was 25-29 years (32.5%) among 852 IUCD acceptors.[15] In addition, data from Chinese national surveys which was conducted by the National Population and Family Planning Committee has shown that in married women aged 15–49 years, there has been an increase in IUCD use from 42.1% in 1988 to 48.0% in 2006[16] that is quite significant. In our study, acceptance of PPIUCD was more common among multiparous (78%) as compared to primis (28%).

Copper IUDS are often associated with an increased amount of menstrual bleeding. Pareek and Gandhi reported an excessive bleeding rate of 6.6% with cesarean insertions.[17] Shukla et al indicated a

higher incidence of menorrhagia (27.2%) with use of Copper T 200 as interval insertion.[18] While Gupta et al observed bleeding in only 4.3% PPIUCD cases using Copper T 380A.[19] Welkovic et al studied postpartum bleeding and infection after post-placental IUD insertion, and found no difference in the incidence of excessive bleeding.[8,20] Difference in types of IUCD could possibly explain the different rates of bleeding problems. The present study showed no significant association of menstrual complaints with the route of insertion and significant menorrhagia at the end of 6 months which was only 6.6%.

Women with IUCDs are more apprehensive regarding the symptom of vaginal discharge. In women reporting with symptoms of unusual discharge actual infection was extremely low on clinical evaluation. A multicentric study from India reported an overall infection rate of 4.5% with PPIUCD.[21] Welkovic et al compared the infection rate among IUCD users and non-users and found no difference.[20] Present study showed only 1.8% vaginal discharge and there was no significant association between vaginal discharge and route of insertion.

A study by Eroglu K et al expulsion rates are higher with postpartum insertion (within 48 hours of delivery) than immediate post placental insertion (within 10 minutes of placental delivery).[22] UN POPIN report stated 6 month cumulative expulsion rate of 9% for post placental compared with 37 % for postpartum insertions.[23] Another study by Celen et al in 2003 had 11.3 per cent cumulative expulsion rate for CuT 300B.[24, 19] Gupta et al reported lower expulsions after cesarean insertions than vaginal delivery. In the present study we had no expulsion in the cesarean group while 03 cases of expulsion occurred in the vaginal delivery group. Still we have a commendable IUCD continuation rate of 97%. This has emphasis on the correct fundal placement of the device and avoiding downward displacement both during vaginal and cesarean insertions.

Perforation of the uterus is uncommon: estimates in larger studies range from 0.4 to 1.6 per 1,000 insertions.[9,12,25,26,27] In the present study, there was no case of perforation or failed IUCD as the uterine wall is thick after delivery and uterine perforation is unlikely to occur during postpartum period.

One of the main observations at follow up was the missing strings. Although nelson A et al.[28] found the strings in all the 7 intra-cesarean inserted IUCD cases. Turan et al also reported missing string rate in interval IUCD insertion to be on the higher side that is 15.6%.[16] Present study showed the significantly high occurrence of missing strings with postpartum IUCD (34%). This was significantly higher with cesarean placements than with vaginal insertions (40% versus 28%). However ultrasound done showed PPIUCD insitu and counseling and reassurance encouraged them to continue with the device.

74 % of mothers were satisfied with PPIUCD in vaginal group and 72 % in cesarean group (p = 0.750) which was comparable to the study by Levi. E. et al. on 90 patients undergoing cesarean delivery. 47 % of women were reached for phone follow-up at 6 months post-partum, and 80 % reported being ''happy'' or ''very happy'' with their IUD. [29]

In conclusion, immediate post-partum insertion of IUD appears to be safe and effective method of contraception in any mode of delivery, both caesarian as well as vaginal. The method may be particularly beneficial in our setting where women do not come for post-natal contraception counseling and usage, resources are less, follow up is poor, literacy is low and awareness about family planning needs further to be done.

Limitation of the study:

The limitations of the study is a small sample size and the duration of the study (6 months only) which both may be increased in further studies to see the long term effect of this procedure in our population.

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SOCIO-DEMOGRAPHIC DISTRIBUTION AND CD4 COUNT PATTERN OF ART-NAÏVE HIV PATIENTS

Muhammad Iqbal Javaid, Muneeza Natiq, Hafiz Muhammad Nuheel Iqbal, Sajjad Haider, Seema Mazhar, Masuma Ghazanfar, Rabia Ahmad, Rizwana Nawaz and Ambereen Anwar

Assistant Professor, Associate Professor, Professor, Department of Pathology, Allama Iqbal Medical College Lahore

Abstract

Gender, socioeconomic status, cultural factors, and age are vital factors constituting susceptibility to HIV, HIV causes the destruction of CD4 helper T lymphocytes both in peripheral blood and lymphoid tissues.4 Estimation of CD4 count is an essential parameter for staging and monitoring the disease progression. This study determines socio-demographic features distribution and CD4 count pattern in treatment naive HIV patients. The findings could help to formulate policy and practices regarding safe treatment of patients by ART to reduce the morbidity of such patient.

Objectives: This study determines socio-demographic features distribution and CD4 count pattern in ART naive HIV patients

Method: One hundred six (106) HIV patients had been enrolled. Data relating socio-demographic factors like age, gender, marital status and income status etc were entered on pre-designed structured proforma. CD-4 lymphocyte count was evaluated on BD FACS Calibur, "an automated four colour" flowcytometer which performs both cell sorting and analysis. Chi-square and ANOVA tests were used for comparison of proportions and means. A p- value <0.05 was taken as statistically significant.

Results: Mean age of subjects included in the study was 31.4 ± 8.5 with the range of 18 and 65 years Sixty-five (61.3%) of the study population was married followed by 41(38.7%) unmarried cases. Out of the 106 subjects there were 83 (78.3%) males, 17 (16%) female patients and 6 (5.7%) trans-gender. Overall, CD4 count mean was of 480.7±298.7cells/µl with a mean of 504.5±315.1 cells/µl and 369.5±213.4 cells/µl in males and females respectively. There was a statistically significant difference in CD4 counts among marital status and income groups with P value <0.05.

Key Words: HIV, Sociodemographic features, CD4 count, ART

The human immunodeficiency virus (HIV) is retrovirus that infects, destroys and paralyzes the immune system of human body. As the infection advances the immune system is no longer able to resist the infections. It can take years to develop full blown disease called AIDS.[1]

Sociodemographic factors comprised five variables: gender, place of residence, level of education, geopolitical zone, and socio-economic status.[2]

In response to the rising incidence of HIV infection among young people, Obidoa, M'Lan, & Schensul noted that public health research has begun to focus on identifying the sociodemographic factors affecting the behavior of young people.[2]

Gender, socioeconomic status, cultural factors, and age are vital factors constituting susceptibility to HIV and that awareness of the risks and knowledge about HIV is essential to translate into positive behavioral change.[3]

HIV causes the destruction of CD4 helper T lymphocytes both in peripheral blood and lymphoid tissues.[4] Estimation of CD4 count is an essential parameter for staging and monitoring the disease progression.[5] CD4 count assess the severity of immune dysfunction. CD4 T lymphocyte count is the number of CD4 T cell per micro liter of blood. It assesses the risk of opportunistic infections, prognosis and guides the physician when to start the antiretroviral drugs.[6]

HIV classification was done by U.S Center for

Disease Control and prevention (CDC) and World Health Organization (WHO). In 1993 CDC revised staging system that assesses severity of HIV infection by CD4 lymphocyte cell counts and specific HIV-related ailments.[7]

CDC staging system is based on 3 ranges of CD4 lymphocytes counts or CD4 percentage and 3 clinical condition. This help clinicians to look at HIV infection as a spectrum of disease starting from acute onset to advanced disease and it is important in AIDS surveillance.[8]

HIV/AIDS pandemic is a major public health problem and recently emerged as an epidemic in Pakistan. It is not only a medical problem but social stigma as well. The basic data about HIV/AIDS is still not available. This issue needs special consideration with reference to diagnosis, treatment and monitoring of the disease.

This study determines socio-demographic features distribution and CD4 count pattern in treatment naive HIV patients. The findings could help to formulate policy and practices regarding safe treatment of patients by ART to reduce the morbidity of such patient. No such study has been conducted to determine pattern of CD4 count and socio-demographic features.

This study determines socio-demographic features distribution and CD4 count pattern in ART naive HIV patients

METHODS

It was Descriptive / Cross sectional study carried out in the Department of Pathology Allama Iqbal Medical College, Lahore. A sum of 106 diagnosed subjects of HIV infection with all genders and age range of 18-65 years were enrolled in the current study.

Sampling Techniques

Non-probability / purposive sampling

Inclusion Criteria

1. HIV positive subjects diagnosed for first time by ELISA and confirmed by Western Blot referred from Punjab AIDS Control Programme.

Exclusion Criteria

1. Self-reporting patients of HIV/AIDS
2. HIV Positive subjects with documented evidence of any other immunological disorder that lower CD4- counts.
3. Patients on antiretroviral therapy (ART)

Immunological categorization of cases was done as per CDC classification system.

- CD4+ T lymphocyte count ≥500/µl
- CD4+ T lymphocyte count 200 – 499/µl
- CD4+ T lymphocyte count <200/µl

Data relating socio-demographic factors like age, gender, marital status and income status etc were entered on 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 was evaluated on BD FACS Calibur, "an automated four colour" flow cytometer 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.

Statistical Analysis

Data was analyzed in software SPSS 23. Frequencies, percentages, mean and SD (standard deviation) were calculated. Cross tabulations were carried out. Comparison of CD4 counts with other variables was done. Chi-square and ANOVA tests were used for comparison of proportions and means. A p-value <0.05 was taken as statistically significant.

RESULTS

One hundred & six cases with HIV/AIDS were enrolled in this study fulfilling inclusion and exclusion criteria in department of Pathology, AIMC Lahore.

The frequency and percentage of socio-demographic features like different age groups, gender distribution, marital status, income groups and alcohol intake are given in Table 1.

In Table 1, frequency distribution for income was categorized as Rs:<5000 (Poorest), Rs: 5001-10000 (Poorer), Rs: 10001-30000 (Middle), Rs: 30001-50000 (Richer) and Rs: >50001(Richest).

The minimum and maximum age with their mean and standard deviation of gender groups and marital groups is given in Table 2.

Table 2 shows mean ± SD, maximum, minimum age for male, female, transgender, married and single subjects with HIV

The frequency and percentage of patients were also calculated according to CD4 count: <200 cells/

µl, 200–499 cells/µl and ≥500 cells/µl based on CDC classification (Table 3)

Mean and standard deviation of CD4 count was determined in different sociodemographic groups and their p value was calculated. (Table 4)

There was a statistically significant difference in the mean values of CD4 counts among marital status and income groups with P value of 0.003 and 0.006 (see Table 4).

Frequencies distribution of male, female, trans-gender, income groups, marital groups and alcohol intake was calculated according to CDC classification of CD4 counts (Table 5).

Table 1: *Scio-Demographic Features of all (n=106), HIV/AIDS Subjects*

		Frequency	Percent	P Value
Age (Groups)	18-29	58	54.7%	0.000
	30-39	32	30.2%	
	40-49	10	9.4%	
	>50	6	5.7%	
	Total	106	100.0%	
Gender (Groups)	Male	83	78.3%	0.000
	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%	0.000
	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%	
Alcohol Intake	No	57	53.8%	
	Yes	49	46.2%	
	Total	106	100.0%	

Statistically significant difference was seen in frequencies of marital status and income categories bearing P values of 0.026 and 0.033 (see Table5).

DISCUSSION

The present study aims at recognizing the sociodemographic features of HIV infection which are very important with the continuing rise in the prevalence of HIV disease in an under developed country like Pakistan. In the present study mean age was 31.4 ± 8.5 ranging from 18 to 65 years and the most of the patients 58 (54.7%) were in age group of <30 years. There was male preponderance (83.78%). In a similar study by Sara Jam and coworkers in Iran

Table 2: *Age Distribution among Gender and Marital Status*

		AGE			
		Mean	**Max.**	**Min.**	**SD**
Gender Groups	Male	31.4	65.0	18.0	8.6
	Female	31.2	50.0	20.0	7.9
	Trans-Gender	31.8	50.0	19.0	11.3
	Total	31.4	65.0	18.0	8.6
Marital Status	Married	34.4	65.0	20.0	8.5
	Single	26.7	50.0	18.0	6.3
	Total	31.4	65.0	18.0	8.6

the mean age was 36.3±9.2 years. Of all the patients, 87% (557) were males.[9]

Another study of similar results conducted in India showed that 60% were males and 40% were females. The age of the patients varied from 18 to 64 years. The maximum numbers of patients (59%) were between 21-40 yrs. The mean age of the patients was 37.3 ±12.4 years.[10]

Table 3: *Distribution of CD4 Counts (Immune Suppression) According to CDC Classification*

CD4 count (Immune Suppression)	**Frequency**	**Percent**
< 200/µl	18	17.0
200-499/µl	38	35.8
≥ 500/µl	50	47.2
Total	106	100.0

In the present study, about 61% of the subjects were married while 39% were unmarried. A study conducted by Chatterjee et al showed 10% single and 90% married subjects. Married also included widow, widower and divorced subjects.[11]

About 49% of the study population in the present study had an income between Rs 5001 to Rs 10,000 while per capita monthly income ranged between Rs 1096 to Rs 1825 in the study conducted by Chatterjee et al.[11]

Several studies have shown a significant association between alcohol consumption and risk of being infected with HIV. Alcohol consumption was seen in 46% of the study population in the present study. A study conducted in Brazil in 2017 showed that 98 out of 160 were having alcohol abuse making a percentage of 60%.[12] Similarly a study conducted by Kiwanuka in Uganda concluded that 64% of the Muslim population had alcohol abuse.[13]

This study showed 47% of the population having CD4 count of >500/ul, 36% had count between 200 – 499/ul and 17% had CD4 count of <200/ul. A study conducted by Vajpayee et al showed 36% of the population having CD4 count of

Table 4: *Mean Distribution of CD4 Count in Socio-Demographic Groups*

		CD4 Count				
		Mean	Maximum	Minimum	Standard Deviation	P Value
Age (Groups)	18-29	528.3	1528.0	40.0	315.6	0.83
	30-39	476.8	939.0	27.0	246.9	
	40-49	286.4	880.0	13.0	275.0	
	>50	364.8	897.0	10.0	325.5	
	Total	480.7	1528.0	10	298.7	
Gender Groups	Male	504.5	1528.0	10.0	316.0	0.236
	Female	369.5	880.0	13.0	213.5	
	Trans-Gender	465.5	804.0	238.0	196.9	
	Total	480.7	1528.0	10	298.7	
Marital Status	Married	414.6	939.0	10.0	254.7	0.003
	Single	585.4	1528.0	51.0	334.8	
	Total	480.7	1528.0	10	298.7	
Income Groups	<5000	370.5	897.0	10.0	274.4	0.006
	5001-10000	452.5	1112.0	24.0	282.1	
	10001-30000	706.9	1528.0	218.0	337.0	
	30001-50000	757.0	757.0	757.0	.	
	>50001	804.0	804.0	804.0	.	
	Total	490.3	1528	10.0	312.9	

Table 5: *Frequency Distribution of Scio-Demographic Character and CD4 Count Groups According to CDC Classification*

		CD4 COUNT STAGING				
		<200/µl	**200-499/µl**	**≥500/µl**	**Total**	**P Value**
Age Groups	18-29	6(10.3%)	23(39.7%)	29(50.0%)	58(100%)	0.079
	30-39	6(18.8%)	9(28.1%)	17(53.1%)	32(100%)	
	40-49	5(50.0%)	3(30.0%)	2(20.0%)	10(100%)	
	>50	1(16.7%)	3(50.0%)	2(33.3%)	6(100%)	
	Total	18(17.0%)	38(35.8%)	50(47.2%)	106(100%)	
Gender Groups	Male	15(18.1%)	25(30.1%)	43(51.8%)	83(100%)	0.132
	Female	3(17.6%)	10(58.8%)	4(23.5%)	17(100%)	
	Trans-Gender	0(0.0%)	3(50.0%)	3(50.0%)	6(100%)	
	Total	18(17.0%)	38(35.8%)	50(47.2%)	106(100%)	
Marital Status	Married	14(21.5%)	27(41.5%)	24(36.9%)	65(100%)	0.026
	Single	4(9.8%)	11(26.8%)	26(63.4%)	41(100%)	
	Total	18(17.0%)	38(35.8%)	50(47.2%)	106(100%)	
Income Groups	<5000	9(39.1%)	5(21.7%)	9(39.1%)	23(100%)	0.033
	5001-10000	6(15.0%)	17(42.5%)	17(42.5%)	40(100%)	
	10001-30000	0(0.0%)	4(23.5%)	13(76.5%)	17(100%)	
	30001-50000	0(0.0%)	0(0.0%)	1(100%)	1(100%)	
	>50001	0(0.0%)	0(0.0%)	1(100%)	1(100%)	
	Total	15(18.3%)	26(31.7%)	41(50.0%)	82(100%)	
Alcohol Intake	No	9(15.8%)	25(43.9%)	23(40.4%)	57(100%)	0.172
	Yes	9(18.4%)	13(26.5%)	27(55.1%)	49(100%)	
	Total	18(17.0%)	38(35.8%)	50(47.2%)	106(100%)	

>500 ul, 30% had count between 200 – 499/ul and 33% had count <200/ul.[14]

p-value of 0.003 was seen between the mean value of CD4 count and marital status of HIV patients making it statistically significant. Sun J et al calculated the p-value of 0.0001 between marital status and ART treatment based on CD4 count making it statistically significant.[15]

Mean value of CD4 counts between different income groups showed p-value of <0.05 favoring statistically significant difference between variables. Gowda S in a cross-sectional study in Mysore

district showed a positive correlation between QoL and CD4 count with value of correlation coefficient to be 0.31 and this correlation was statistically significant with $P < 0.05$.[16]

CONCLUSION

Sociodemographic features had an important impact on HIV patients. HIV was found to be more common in young males with predominance among married people. Poor socioeconomic status and alcohol intake were associated with the disease. Majority of the population had CD4 count >500/ul. Statistically significant relationship was found among CD4 count, marital status and different income groups.

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CRITICALLY ILL PATIENTS IN OBSTETRICS AT JINNAH HOSPITAL LAHORE-----OBSTETRICIAN VIEW

Zareen Amjad, Zakir Sial, Muhammad Shahid, Amtullah Zarreen, H.M. Amjad, Zeshan Siddique, Nabila, Maria Shahid, Shomaila, Luqman Sadiq, Warda, Shahid Rafiq, Shehzad Afzal, Rizwan Asma Saleem.

Abstract

Background; Care of critically ill patients is a unique challenge in obstetrics because of its unpredictability. Complications of pregnancy and child birth are the leading cause of death and disability in women of reproductive age. So intensive care provided to critically ill patients is an important aspect of obstetric services delivered in tertiary care. Dedicated ICU for obstetrics patients is not yet widely available in developing countries. Hemorrhage, hypertension, septicemia, medical disorders are leading causes of ICU admission and maternal mortality. Early detection and prompt referral to tertiary centers with ICU facilities can minimize complications and mortality in seriously ill patients.

Objective: To find out the proportion of obstetrics patients admitted, frequency of serious diseases, interventions required in ICU, duration of stay and maternal out come.

Material and methods: Retrospective study carried out in Gynae department of Jinnah Hospital Lahore from May 2014 to May 2017. All patients who were critically ill and required ICU care were included in study. Variable studied were patient's demographic, causes for admission in ICU, ICU stay, Interventions required during stay, outcome in terms of discharge, mortality and long term morbidity.

Results: Total 417 patients admitted in ICU making 1.04% of obstetric admission and 13% of total ICU admissions during last 3 years. Most patients belonged to age group 20-30 years (n=237) 56.8%, less than 20yrs (n=57)13%, More than 30 years (n=123)30%. Primigravida were (n=228)54%, Multigravida (n=156)37.4%, grand multi (n=33)7.9%. Most of admissions were in post partum period (n=348) 83.4%, rest were antenatal (n=69)16.5%. Regarding indications for admission most common indication was eclampsia and its complications (n=228) 54.6%, second common indication were medical disorders(n=69) 16%, followed by obstetric hemorrhage(n=63)15%, sepsis (n=36) 8.6% and surgical causes like RTA (n=15)3.5% respectively. Hospital stay was up to 72 hours in (n=250) 60% of patients, 1 week in (n=100) 20%, 2-3 weeks in (n=42) 10% and (n=22) 5% patients requiring stay up to 90 days. During stay (n=318) 76% required ventilator support, 26% (n=111) had dialysis, tracheotomy done in 5% of patients. In addition, 30 % (n= 110) required blood transfusion and 20 % (n= 108) ionotropic support with other interventions. 33% patients expired, 64% were discharged and 3% got LAMA.

Conclusion: Most admissions were done due to Eclampsia and its complications. These can be reduced by providing good antenatal care at remote areas, eclampsia management suits at DHQs and THQs so that referral can be reduced to tertiary care hospitals. Highest cause of mortality was sepsis which can be reduced by providing optimum facilities for child birth at remote areas.

Our study was comparable with study done at Bangladesh where Obstetrics admissions were 0.8% of total obstetric admission and 14% of ICU admission. Whereas in Armed Forces Institute Hospital in Riyadh it was 0.2% of total deliveries and 1.6% of ICU admissions which are comparable to developed countries. While in INDIA, Results are varying.

It has been reported that modern intensive or critical care medicine emerged in the 1950s, largely pioneered by the anesthetist, Dr. Bjorn Ibsen during the polio epidemic at the Kommune hospital in Copenhagen in 1953.[1] Pregnancy requiring critical care is not only challenging for obstetrician

Correspondence: Dr. Zareen Amjad, Department of Obstetrics and Gynaecology, Allama Iqbal Medical College, Lahore, E-mail : drzareenamjad99@gmail.com

but also a unique cohort for intensivist. Critically ill patients are those who have acute life threatening complications.[2] Difficulties are encountered in management of these patients as it is matter of two lives, moreover physiological changes of pregnancy may compromise and hinder the responses required to combat the disease. Admissions of obstetric patients requiring intensive care occur in 0.07-0.9% of cases in developed countries and for developing countries it can be upto 10%.[3]

Developed countries are using near miss mortality or severe acute maternal morbidity (SAMM) analysis as a tool for monitoring the quality of maternal health services. Different indicators are being used to assess SAMM. Recent systemic review of maternal morbidity and mortality by WHO has taken transfer to ICU as an indicator to assess prevalence of SAMM[4]

Hypertension in pregnancy, hemorrhage and sepsis are major causes for maternal morbidity and ICU admission in Asia. 99% of global maternal mortality is prevalent in developing countries.[5] We have failed to achieve millennium development goal regarding woman health. WHO report says 1 out of 16 women in Africa faces a lifetime risk of maternal death compared to 1 in 65 in Asia, 1 in 130 in Latin America and just 1 in 1400 in Europe and 1 in 3700 in North America.[6]

A lot of improvement being carried out in providing health care to women but still maternal morbidity and mortality remain high due to lack of provision of antenatal care for high risk pregnancies. Poverty, lack of education, inadequate transport system is barriers to get optimal antenatal care.[7]

Management of critically ill pregnant lady demands multidisciplinary approach requiring obstetrician, anesthetist and intensivist. Provision of ICU to critically ill patients is a notion to save maternal life .Fetal mortality also eminent due to severe maternal illness, maternal shock, and absence of prenatal care and prematurity.[8]

In developing countries ICU facilities are not accessible to all women so data regarding incidence, risk factors, course and outcome of obstetrical patients requiring ICU care is lacking. In Pakistan data is almost nonexistent. Being vigilant in peripartum period in high risk pregnancies concede earlier detection of maternal complications and their management through multidisciplinary approach. So analysis of critically ill obstetric patients is desired to amend future pregnancy outcome.[9]

METHOD

This study carried out at Jinnah hospital Lahore. It is 1500 bedded hospital with three ICU facilities, but dedicated obstetric ICU is still lacking. This study conducted for a period about three years and four months from May 2014 to September 2017. All patients who were critically ill and required ICU care included in study. Variable studied were patient's demographic, causes for admission in ICU, ICU stay, Interventions required during stay, outcome in terms of discharge, mortality and long term morbidity.

RESULTS

Out of 40000 deliveries, 417 obstetric patients were admitted in ICU that constitutes 1.04% of obstetric admissions. Total ICU admissions during this period were 3200 patients. Out of total 3200 ICU admission, 417 patients were obstetric admissions that constitute 13.2% of total ICU admission during this period.

Table 1: *Demographic Characteristics of Patients*

Characteristics	Number	%(Total 417)
Age(Years)		
Less than 20	57	13
20-30	237	56.8
More than 30	123	29.4
Parity		
Primipara	228	54.6
Multipara	156	37.4
Grandmultipara	33	7.9
Time of admission		
Antepartum	69	16.5
Postpartum	348	83.4

Table 2: *Indication for Admission in ICU*

Factors	Total pts	%
Hypertension in Pregnancy	228	54.6
Morbid adherence of Placenta	48	11.5 (Obstetric Heamorrhage)
Abruption	15	3.5 (Obstetric Heamorrhage)
Sepsis	36	8.6
Medical disorders	69	16.5
Road traffic accidents(RTA)	15	3.5

Table 3: *Breakdown of Indications for ICU Admission*

Condition at admission	Number-228	%
3a-- Hypertensive disorders		
Eclampsia	205	89.9
HELLP	15	6.5
Intracranial heamorrhage	5	2.19
Posterior reversible encephalopathy syndrome	2	0.87
Cortical thrombosis	1	0.4%
3b- Breakdown of PPH		
Obstetric hemorrhage	N=63	%
Uterine atony	10	15.8
Ruptured uterus	8	12.6
Morbid adherence of placenta	45	71.4
3C- Breakdown of Medical disorders		
Medical disorder	N=69	%
DIC	7	11.4%
Pulmonary embolism	10	14.7%
Peripartum cardiomyopathy	15	22%
Pulmonary oedema	22	32.3%
Hepatic failure	9	13.2%
Tuberculosis meningitis	6	8.8%

Table 4: *Interventions in ICU*

Interventions	Number	%
Blood and blood products	110	26.3
Mechanicle ventilation	318	76
Dialysis	111	26
Tracheostomy	21	5
Ionotropic support	108	25.8
Surgery	15	3.5

Table 5: *Duration of ICU Stay:*

Stay in ICU	Number	%
24 -72 hours	250	60
7 days	100	24
1 month	42	11
3 months	22	5

Table 6: *Outcome of Patients*

Outcome	Number	%
Discharged	267	64
Expired	138	33
LAMA	12	3

Table 7: *Diagnosis in Patients Expired*

Diagnosis	Number(138)	%
Hypertension complications	66	47.8
Hemorrhage	21	15.2
Sepsis	18	13
Medical disorder	27	19.5
Complication of surgeries done in ICU/RTA	6	4.34

Table 8: *Breakdown of Patients with Diagnosis and Outcome Regarding Mortality*

Diagnosis	Total	Expired	Recovered
Hypertensive complications	228	66(28.9%)	160(70%)
Hemorrhage	63	21(33.33%)	42(66%)
Medical	69	27(39.15%)	42(61%)
Sepsis	36	18 (50%)	18 (50%)

DISCUSSION

Care of critically ill patient is a unique challenge in obstetrics particularly because of its unpredictability. Hemorrhage, toxemia, anemia and sepsis are most common complications encountered in patients requiring ICU care. Obstetric care in developing countries is different from developed countries. In our study total admissions carried out in ICU were 1.04% that is 1 in 100 deliveries .It is comparable to study carried out at Ayyub Medical College in 2008 where admission in ICU were 1.34%.[10] A study conducted in New Delhi, India by Tripathi et al showed that the rate of obstetric admissions in ICU admission was 1 in 540 deliveries. Obstetric admissions were 13 % of general ICU admissions (from different disciplines) similar to a study carried out at Bangladesh where it was 14% of total patients admitted in ICU.[11,12] But results differ from study carried out at King Abdullah Hospital where admission rate was 0.2% i.e. 2 in 1000 deliveries and 1.6% of total ICU admissions which were comparable to rates in developed countries.[13] American academy of family physicians had mentioned 0.4% admissions of the total deliveries.[14] Mabie and Sibai reported that

1% of women delivered at the University of Tennessee were admitted to Obstetrical ICU.[15] Only 0.4% of obstetrical patients needed ICU treatment in a study by Harris & Foley at the University of California, San Fransico.[16] Niyaz et al reported obstetric patients accounts for 0.41% of all ICU admission.[17] These variations might be due to differences in defining major morbidity criteria for ICU admission & availability of high dependency unit (HDU), an intermediate care unit.

Majority of admissions were in postpartum periods that constitutes n=348 (83.4%) patients which is comparable to study carried out by Lataifeh et al.[13] Our study showed that hypertension and its complications were leading causes for admissions to ICU. About(n=228)(54.6%) patients were admitted in ICU due to hypertension and its sequalae. Two rare complications of hypertension, cortical thrombosis and posterior reversible encephalopathy syndrome (PRES) were also noted .Eclampsia was most prevalent among hypertension (n=205) 89.90%. A study carried out at turkey and many other studies showed that eclampsia was most common cause for ICU admission and mechanical ventilation.[18] In developing countries eclampsia is still common due to lack of antenatal care and many patients' presents with advanced complications like cereberovascular accidents, pulmonary oedema, cardiovascular compromise due to recurrent fits. Eclampsia accounts for up to 12% of deaths during pregnancy. ICU care can help to reduce maternal mortality and morbidity.[19]

Second most common cause requiring ICU admission were medical disorders other than hypertension (n=69)(16.5%) immediately followed by obstetric hemorrhage(n=63) (15%). This aspect of our study was different from many studies as medical disorders were not much common and most patients admitted in ICU were having obstetric hemorrhage and its complications like DIC (disseminated intravascular coagulation) and ATN(acute tubular necrosis). Among medical disorders liver diseases, cardiomyopathies, meningitis and encephalitis were seen and required medical ICU care. Poor prognosis seen in patients with fulminant hepatic failure.[20]

Third most common cause of ICU admissions in our study was obstetric hemorrhage and its complications. Most common risk factor for obstetric hemorrhage was morbid adherence of placenta 45(71%) which is due to high cesarean section rate. Patients admitted in ICU for ionotropic supports and mechanical ventilation. In contrast to other studies (Tang et al and Sharma showed highest admission rate due to PPH) admissions rate in ICU due to PPH heamorrhage was less in our study.[21,22] The reason could be that these cases were well managed in time and replacement of blood and blood products done adequately though there is no separate blood bank for labor room in our hospital but we managed to arrange blood with great efforts of our house officers and trainees.

Sepsis is major cause of maternal mortality and morbidity in developing countries. In our study (n=36) (8.6%) patients were admitted with sepsis. It was due to mismanaged labor and delivery outside hospital, non adherence to operation theatre and sterilization protocols, patients' poor hygiene, anemia and malnourishment and unavailability of broad spectrum antibiotics in hospital. Patients required ICU care and mechanical ventilation due to pulmonary edema and ARDS (Adult respiratory distress syndrome) as a result of sepsis.[23]

RTA is not uncommon in pregnancy. Fetal death rates of 57% and maternal death rate of 8-16% are reported in developed countries while in developing countries data is nonexistent. Limb fractures, pelvic bone fracture, quadriplegia, uterine rupture, abruption placenta, lacerations, etc are common injuries encountered in RTA. 3.5% of our patients got serious injuries during pregnancy and got admitted in ICU. Most of them encountered head injuries and required mechanical ventilation.[24]

Regarding intervention carried out in ICU 76% patients required ventilation. Patients having eclampsia complications were at top requiring ventilatory support. Pulmonary edema, ARDS and pulmonary

embolism were common among respiratory problems. This is comparable to study carried out by Pattanik et al where mechanical ventilation required in 72% of patients.[25] Dialysis required in 26% of patients. Most studies didn't mentioned dialysis except Pattanik et al where only 7.4% patients required dialysis and Niayaz et al stated that 1 patient required renal transplant.[11,12,18,20,25,26] Blood transfusion done in 26% of patients. Ionotropic supports required in 25%. It was about half of that observed by study carried out by Fatima et al at turkey where Blood transfusion done in 50% of patients.[18] Tracheostomy done in 5% of patients. 3.5% patients required surgery after admission in ICU like drainage of cranial hematoma, surgery for burst abdomen and resection anastomosis of gut. This aspect was not mentioned in other studies carried out.

60% patients had stay in ICU upto 72 hours. 5% patients had admission duration in ICU for 90 days. This was also unique to our study as other studies showed ICU stay for 72 hours maximum except a study carried out at Kerala hospital India where maximum stay in ICU was 30 days in few patients.[9,10,11,12,13,18,27]

Out of 417 admissions in ICU 267(64%) patients treated and discharged from ICU,138 (33%) expired, 12(3%) left against medical advice. Mortality rate was quiet high as compared to other studies but comparable to study carried out at north kerala India where 34% patients expired and local study carried out at Ayyub Medical college that show mortality rate of exactly 33%. It is evidant that we are still lagging behind to reduce maternal mortality in spite of development of health system infrastructure.[27,10]

Further breaking down the data to view the causes of maternal mortality it was seen that mortality was highest (50%) in patients with sepsis. Good prognosis seen in patients presenting with eclampsia and hypertension. 70% of these recovered and 30% expired. While regarding obstetric heamorrhage 2/3rd (66%) patients revived and 1/3rd (33%) expired. In medical disorder ratio of recovery and mortality was 60:40. It is apparent that sepsis was major killer. It is contrary to studies carried out in developing countries where sepsis rate and hence mortality was quiet low but two studies from India showed mortality due to sepsis 25% and 27% respectively.[27,28] It is half of that observed in our study. Studies from Iran and Turkey showed sepsis rate and mortality less than 1%. [18,29]

CONCLUSION

Accessibility to good obstetric care is the basis for decreasing maternal mortality. In our country high number of women delivers at home or in basic health units so there is a need for a regional referral center to respond to emergency situations. Provision of access to the ICU is an important aspect of care and is a measure of the quality of obstetric care delivered. For some women provision of this care is a matter of life and death. Sepsis is major avertable cause of maternal mortality and morbidity. Sepsis is understated so its role in maternal mortality remains hindered. Strict adherence to infection control protocols in hospital and treating antenatal risk factors for sepsis can play an assertive role in reducing mortality. Early recognition of hypertension and risk factors for hemorrhage and their aggressive management is required. To circumvent any delay in referral or shifting to ICU it is desired to institute a dedicated obstetric ICU in tertiary hospitals.

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EASE OF LMA INSERTION WITH SEVOFLURANE PLUS PROPOFOL VERSUS PROPOFOL ALONE IN ADULT PATIENTS

Sajjad Hussain[1], Muhammad Naveed[2], Azhar, Aamir Bashir[3]

[1]Assistant Consultant Anesthesia, Dr. Suleiman AL Habib Hospital, Rayan Branch Riyadh, KSA; [2]Registrar Anesthesia & Intensive care, University Hospital Waterford Dunmore road, Waterford Ireland; [3]Assistant Professor, Anesthesia Shalamar Medical & Dental College, Lahore

Abstract

Background: Laryngeal mask airway (LMA) is commonly used for management of airway in general anesthesia. It provides ease of insertion for the placement in the pharynx where it forms a low-pressure seal around the laryngeal inlet. Different anesthetic agents are used for induction of anesthesia for LMA insertion.

Objectives: To compare the efficacy of sevoflurane plus propofol with propofol alone for ease of laryngeal mask airway insertion in adult patients for elective surgery.

Study Design: Randomized clinical trials.

Place and duration of study: Operation theatre, Shaukat Khanum Memorial Cancer Hospital & Research Center, Lahore over a period of six months.

Material and methods: A total of 100 patients i.e. 50 patients in each group included in study. Demographic data noted. Participants were assigned to receive sevoflurane plus propofol (Group-A) and propofol alone (Group-B) as their anesthetics, airway managed with LMA and efficacy was considered LMA insertion in first attempt. Data were analyzed using SPSS (version 11). The two groups were compared for efficacy using chi square test. p-value of ≤0.05 was considered significant.

Results: 100 patients were analyzed: 50 patients in each group. No significant demographic differences. Efficacy of ease of LMA insertion was 88% (n:44) in group A while 78% (n:39) in group B, with p-value 0.000

Conclusion: There are more chances of successfull LMA insertion with sevoflurane plus propofol than propofol alone in adult patients for elective surgery.

Key words: Laryngeal mask airway, Sevoflurane, Propofol

Laryngeal mask airway (LMA) is commonly used for management of airway in general anesthesia It provides ease of insertion for the placement in the pharynx where it forms a low-pressure seal around the laryngeal inlet. LMA is available in different sizes and also have the option to be used for the placement of bronchoscope.[1,2] Different anesthetic agents are used for induction of general anesthesia for LMA insertion. Propofol premixed with lignocaine has the advantage of inducing anesthesia rapidly and suppressing airway reflexes. It may be associated with certain side effects like pain on injection, apnea, and hypotension. [3,)]

Sevoflurane is an inhalational anesthetic with low blood gas solubility coefficient, is also a suitable choice at 8% dial concentration for vital capacity breath at a fresh gas flow of 6 lit per min of oxygen. It provides better hemodynamic stability and is associated with less incidence of apnea as compare to propofol. However, it requires longer time for LMA insertion as compared to propofol.[5]

LMA was invented by Dr Archie IJ Brain, a British Anesthesiologist at London Royal Hospital in 1981. It fills the gap in airway management

Correspondence: Dr. Sajjad Hussain, Assistant Consultant Anesthesia, Dr. Suleiman AL Habib Hospital, Rayan branch Riyadh, KSA. Email: drsajjadskm@gmail.com

between tracheal intubation and use of the face mask. It allows the administration of inhaled anesthetics through a minimally stimulating airway. The increasing emphasis on day care anesthesia has led to the greater use of LMA as an alternative to the face mask and in some cases to tracheal intubation. Since its introduction, various induction agents namely thiopentone, propofol, halothane, sevoflurane have been used for induction of anesthesia for laryngeal mask airway placement. Satisfactory insertion of the laryngeal mask airway after induction of anesthesia requires sufficient depth for suppression of airway reflexes and to avoid untoward effects due to airway instrumentation.[6]

Propofol with or without an opioid has been used as the induction agent of choice for LMA insertion as it provides better pharyngeal and laryngeal relaxation, depressing upper airway reflexes, and also has a favorable recovery profile with low incidence of side effects. However, it is by no means ideal, as it is associated with significant adverse effects like pain on injection and cardiovascular and respiratory depression (hypotension, apnea).[7]

Sevoflurane, a halogenated volatile anesthetic agent, with pleasant odor is non-irritating to the airways and is suitable for inhalation induction for both children and adults. It is also associated with a very low incidence of breath holding, coughing, and laryngospasm. In addition, its low lipid solubility (blood/gas partition coefficient at 37°c is (0.63-0.69) allows a rapid and smooth induction, quick adjustments of anesthetic depth, maintenance, rapid elimination, good hemodynamic stability, and a predictably short recovery suitable for day care anesthesia.[8]

OBJECTIVES

To compare the efficacy of sevoflurane plus propofol with propofol alone for ease of laryngeal mask airway insertion in adult patients for elective surgery.

STUDY DESIGN: Randomized clinical trials.

PLACE AND DURATION OF STUDY:

Operation theatre, Shaukat Khanum Memorial Cancer Hospital & Research Center, Lahore over a period of six months.

SAMPLE SIZE: Calculated sample size was 100 i.e. 50 cases in each group with 1% margin of error, 80% power of study taken expected percentage of successful LMA insertion, 93.5% in sevoflurane plus propofol and 61.5% in patients with propofol alone.

Groups were as followed: **Group A:** Sevoflurane plus propofol and **Group B:** Propofol alone

SAMPLING TECHNIQUE: Non-probability purposive sampling.

SAMPLE SELECTION: Patient from elective surgery list aged 18-60 years of either gender, having American Society of Anesthesiologist (ASA) status I and II, undergoing minor surgical procedures like cystoscopy, EUA, excision of breast lump etc. were included in study. However, patients refusing consent, emergency cases, patients at risk of pulmonary aspiration, patients with known hypersensitivity to propofol or sevoflurane and patients with anticipated difficult airway were excluded from the study.

DATA COLLECTION PROCEDURE: After approval of Shaukat Khanum Hospital Ethical Committee and informed written consent, a total of 100 patients i.e. 50 patients in each group selected from elective surgery list fulfilling the inclusion criteria were included in the study. Patient's demographics were noted. By using lottery method, the participants were assigned to receive sevoflurane plus propofol (Group-A) and propofol alone (Group-B).

No patient was pre-medicated. Procedure was started by concerned doctor. Patients were pre-oxygenated with 100% oxygen for 3 minutes. Patients in group-A received induction with propofol 1.5 mg/kg intravenously premixed with lignocaine 1% (1 mg lignocaine/10 mg propofol) given over 30 seconds along with sevoflurane with 8% dial concentration in a 2:1 of nitrous oxide to oxygen and fresh gas flow of 6 L/min. Patients in Group-B received induction with propofol 3mg/kg intrave-

nously premixed with lignocaine1% (1 mg lignocaine/10 mg propofol) given over 30 seconds. The start of induction was taken as the patient completed a single vital capacity breath. The patient was asked to open the eyes after 10 seconds. Failure to do so was taken as loss of unconsciousness. 30 seconds after completion of propofol induction, LMA insertion was attempted. Efficacy was considered when LMA insertion was full.

Full: Smooth LMA insertion (loss of eye lash reflex and mouth opening) in first attempt.

Partial: When insertion was accompanied by gag reflex, coughing or involuntary movements.

Poor: When LMA insertion was impossible.

If mouth opening was impossible, attempts were repeated up to 4 times. Oxygen was given in between attempts. Each attempt preceded by propofol bolus 0.5mg/Kg.

Failure of insertion of LMA after 4 times was rescued with succinylcholine 25 mg intravenously. Non-invasive arterial blood pressure, O2 saturation and heart rate was recorded every minute for 05 minutes as both propofol and sevoflurane cause hypotension and apnea so these parameters was monitored. An independent observer observed loss of eye lash reflex along with jaw relaxation. Efficacy was considered if there was full LMA insertion.

DATA ANALYSIS

Data was analyzed using SPSS (version 11). Mean and standard deviation was calculated for age Frequency and percentage were calculated for gender and efficacy. The two groups were compared for efficacy (for efficacy see operational definition) using chi square test. P≤0.05 was considered statistically significant.

RESULTS

100 patients were analyzed: 50 patients in Group-A and 50 patients in Group-B.

In Group A, mean age is 42.42±9.97 and in Group- B mean age is 41.66±10.30

In Group A, 74% patients are male and 26% female and in Group B 56% patients are male and 44% female. The frequency of LMA insertion at first attempt was successful as:

- Group A: 44 out of 50 patients i.e.: 88%
- Group B: 39 out of 50 patients i.e.: 78%

This shows higher frequency of successful LMA insertion at first attempt in Group A patients, with p-value of 0.000

DISCUSSION

Our present report shows that after induction of anesthesia in Group-A the percentage of successful LMA insertion at the first attempt was 88% and group B was 78%. Our results are comparable to those achieved by Sayyed SMS "Comparison of sevoflurane plus propofol versus sevoflurane or propofol for laryngeal mask airway insertion in adults" who showed incidence of successful LMA insertion at first attempt 93.5% in patents induced with 8% sevoflurane and supplemented by propofol and 61.5% in patients induced with 3mg/kg propofol.[9]

Table 1: Demographic Data

Group	Age (Mean + SD)	Gender	
		Male	Female
A (n:50)	42.42±9.97	74% (n: 37)	26% (n:13)
B (n:50)	41.66±10.30	56% (n:28)	44% (n:22)

Table 2: Ease of LMA Insertion

Group	Successful LMA insertion	Frequency (n)	Percentage %	P Value
A (n:50)	Yes	44	**88%**	0.000
	No	6	12%	
B (n:50)	Yes	39	**78%**	
	No	11	22%	

In our patients of Group-A there was prolonged time to jaw relaxation as compared to Group-B patients. Some extra attempts of LMA insertion were required in Group-B patient and also required additional doses of propofol. Our reports show that anesthetic induction with propofol plus sevoflurane resulted in larger number of successful LMA insertion at first attempt as compared to patients induced with propofol alone.

Scanlon P et al concluded propofol a better choice than thiopentone for insertion of LMA in two

groups of ASA I patients.[10] In another study conducted by Fedman B, sevoflurane was found a comparable choice to propofol for ambulatory anesthesia.[11] However, a randomized trial conducted by Thwaties A et al, induction of general anesthesia was slower with sevoflurane when compared with propofol.[12] Another study conducted by Sivalingam P et al concluded that addition of alfentanil to either propofol or sevoflurane provided better conditions for LMA insertion.[13]

Molloy ME et al found sevoflurane requires more time when compared with propofol for smooth insertion of LMA.[14] A meta-analysis conducted by Joo HS et al concluded propofol as an ideal induction agent to induce general anesthesia.[15] Priya V et al did not found statistically significant difference on LMA insertion with propofol or sevoflurane, how-ever patients receiving propofol were found more comfortable.[16]

CONCLUSION

We concluded that, there are more chances of successfull LMA insertion with sevoflurane plus propofol than propofol alone in adult patients for elective surgery.

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THYROID DYSFUNCTION AMONG TREATMENT NAÏVE PATIENTS OF HUMAN IMMUNODEFICIENCY VIRUS PRESENTING TO HIV CLINIC OF A TERTIARY CARE HOSPITAL IN LAHORE PUNJAB

Samina Saeed, Sadaf Iqbal, M. Abbas Raza, Zaid Tayyab, Nadeem Hussain, Mahmood Nasir Malik, Emaan Salam

Associate Professor, Senior Registrar, PGR, Professor, Department of Medicine, Jinnah Hospital, Lahore

Abstract

Background: HIV infection exists as a concentrated epidemic in Pakistan meaning that the prevalence in traditional risk groups exceeds 5%. So it becomes highly important to address not only the control of this disease but also the issues related to this disease which can improve the quality of life of patients living with HIV.

Objective: The objective of this study was to determine the frequency of thyroid dysfunction among treatment naïve patients of human immunodeficiency virus presenting to HIV clinic of a tertiary care hospital in Lahore Punjab.

Methodology: A cross sectional study enrolling 150 treatment naïve patients of HIV was conducted in HIV clinic Jinnah hospital Lahore. An informed consent was taken from subjects before including them in the study. Venous blood samples were taken and were sent immediately to the pathology laboratory of INMOL hospital Lahore in standard serum vials. The results of thyroid profile were collected next day by the researcher and were noted on a predefined proforma. Confidentiality of the data was ensured. Thyroid dysfunction was labelled as serum TSH concentration of <0.5mU/L or >5.7mU/L determined by radioimmunoassay of the serum of the patient.

Results: Mean age of study participants was 42.02+15.43 years. There was an overall male predominance 79(52.7%). The mean TSH level of the patients was calculated as 2.86+1.5 mIU/L. Thyroid dysfunction was found in 48 (32%) patients of treatment naïve of HIV. Out of 48 patients of thyroid dysfunction there were (56.25%) patients having <0.5mIU/L and(43.75%) patients having TSH >4.5mIU/L. By using chi-square, it was observed that age and gender have no significant association with the presence of thyroid dysfunction having(p-value 0.165 and 0.654 respectively). It was noticed that duration of HIV was significantly associated with the presence of thyroid dysfunction with (pvalue0.001.)

Conclusion: Present research revealed that thyroid dysfunction was found in 32% treatment naïve patients of HIV. Age and gender had no significant association with the presence of thyroid dysfunction but duration of HIV was significantly associated with the presence of thyroid dysfunction.

Keywords: Human Immunodeficiency Virus, Thyroid dysfunction, Thyroid stimulating hormone

A variety of HIV related endocrine dysfunctions including adrenal, gonadal and thyroid disorders have been reported.

In the pre-highly active antiretroviral therapy (HAART) era, this was primarily associated with opportunistic infections such as cytomegalovirus and tuberculosis.

In the era of HAART, a more complex situation has developed, with many patients experiencing insulin resistance, diabetes, sex hormone abnorma-

Correspondence: Dr. Samina Saeed, Associate Professor of medicine, Allama Iqbal Medical College, Lahore.
Email: saminasaeedsaeed1@gmail.com

lities and osteoporosis, with no unifying mechanism established for these conditions. Recently, thyroid dysfunction has been reported[1-8] with a reported increased prevalence of abnormal thyroid function tests, in particular subclinical hypothyroidism in both adults and children on HAART.[2, 6] As a variety of HIV-related endocrine dysfunctions including adrenal, gonadal and thyroid disorders have been reported in literature. This data is relevant when investigating the factors associated with thyroid dysfunction in our HIV positive population.

So the objective of this study was to determine the frequency of thyroid dysfunction among treatment naïve patients of human immunodeficiency virus presenting to HIV clinic of tertiary care hospital.

METHODS

Design and Setting: It was a cross sectional study conducted in HIV Clinic, Jinnah Hospital Lahore in a period from November to February 11, 2016.

Sample Selection: Using non consecutive samp-ling, a total sample size of 150 cases was calculated with 95% confidence level, 8% margin of error and taking expected percentage of thyroid dysfunction as 30%9 (least among all). Treatment naive patients of HIV (diagnosed as having HIV infection determined by PCR for at least one year and without any history of treatment with antiretroviral drugs), irrespective of age and gender, presenting for follow up to HIV clinic of tertiary care hospital, were included in the study. Patients who were taking antiretroviral therapy, already diagnosed as having thyroid dysfunction, patients on drugs affecting thyroid level (i.e. thyroxine, carbamazapine, propylthiouracil), patients with history of total or partial thyroidectomy and those who were not willing to participate in the study were excluded.

Data collection procedure: A total of 150 treatment naïve patients of HIV presenting to HIV clinic of Jinnah Hospital Lahore and fulfilling the selection criteria were approached. An informed consent was taken from patients before including them in the study.

Blood samples (5ml venous blood) were taken by following aseptic measures and standard protocol by the researcher himself. Samples were sent immediately to the pathology laboratory of INMOL hospital, Lahore in standard serum vials. The results of thyroid profile were collected next day by the researcher and were noted in the proforma. Confidentiality of the data was ensured. Thyroid dysfunction was labeled as serum TSH concentration of <0.5 mU/L or >4.5 mU/L determined by radioimmunoassay of the serum of the patient.

Data Analysis: Data was entered and analyzed using SPSS version 17.0. Numerical variable i.e. age, TSH levels were summarized as mean and standard deviation. Qualitative variables like gender, presence of thyroid dysfunction among treatment naïve patients were presented as frequency table. Data was stratified for age, gender and duration of HIV to deal with effect modifiers. Post stratification chi-square test was applied. P-value <0.05 was considered as significant.

RESULTS

Table-1 shows demographic characteristic of patients. Among 150 treatment naïve patients of HIV, it was observed that the minimum age of the patients was 20 years and maximum was 69 years having mean of 42.02+15.43 years. 79(52.7%) patients were male and 71 (47.3%) patients were female.

The minimum TSH level of the patients was calculated as 0.35mIU/L and maximum 5.5mIU/L having mean 2.86+1.5mIU/L. Thyroid dysfunction was found in 48(32%) patients and thyroid dysfunction was not found in 102(68%) treatment naïve patients of HIV as shown in Figure2. Out of 48

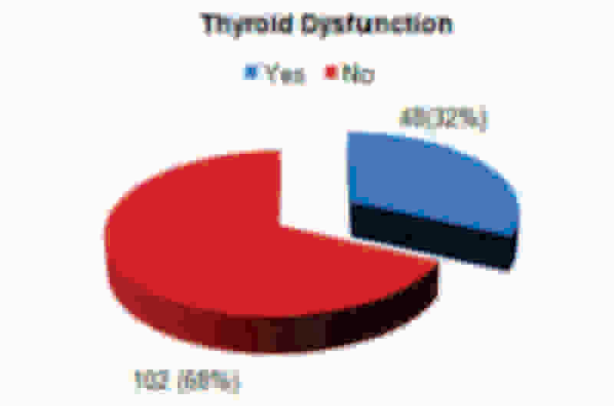
Table 1: Demographic Characteristics

Age (Mean ± S.D) years Range	42.02±15.43 20 - 69
Gender n (%) Males Females	79 (52.7%) 71 (47.3%)

patients of thyroid dysfunction there were 56.25% patients having TSH < 0.5 mIU/L and 43.75% patients having TSH >4.5 mIU/L. By using chi-square, it was observed that age and gender had no significant association. With the presence of thyroid dysfunction having p-value 0.165 and 0.654 respectively but duration of HIV was significantly associated with the presence of thyroid dysfunction with p-value 0.001.

Figure-1. *Frequency of Thyroid Dysfunction in Treatment naïve HIV Positive Patients*

DISCUSSION



The present research was conducted to determine the frequency of thyroid dysfunction among treatment naïve patients of human immunodeficiency virus presenting to HIV clinic of tertiary care hospital. In this regard the present cross sectional study was conducted at HIV clinic, Jinnah hospital Lahore. So 150 treatment naïve patients of human immunodeficiency virus were included after fulfilling the inclusion and exclusion criteria by using non probability consecutive sampling. In present research, among 150 treatment naïve patients of HIV, having mean of age 42.02 + 15.43 years, 52.7% were male while 47.3% were female patients. The mean duration of HIV was calculated as 13.34 + 5.17 months.48(32%) patients had thyroid dysfunction, Out of these 48 patients of thyroid dysfunction 56.25% patients had TSH < 0.5 mIU/L and 43.75% patients had TSH > 4.5 mIU/L.

Table 2: Association of Thyroid Dysfunction with Different Study Variables

Variables	Thyroid Dysfunction			p-value
	Yes	No	Total	
Age < 40 years > 40 years	21 27	57 45	78 72	0.165
Gender Male Female	24 24	55 47	79 71	0.654
HIV Duration < 18 months > 18 months	24 24	84 18	108 42	0.

Our research revealed that thyroid dysfunction was found in 48(32%) patients and thyroid dysfunction was not found in102(68%) of treatment naïve of HIV. These results agree to the study results of Nishaut et al. This study was done in 210 newly diagnosed HIV positive patients having CD4 count 180-330 cells/mm^3 showing thyroid dysfunction in 75.5 % Vs 16% patients in control group(p<.0001)

The results of another study done by Noureldeen et al on 100 patients showed that 70 cases(70%) in treatment naive HIV infected patients had normal thyroid function tests when compared with control individuals, while 30 cases(30%) of HIV infected patients had abnormal thyroid function. Of the 30 cases, 11(11 %)cases had abnormal TSH values, with increased TSH (7cases), decreased TSH (4 cases), hypothyroidism (subclinical and overt: 6 cases and 1 case respectively), hyperthyroidism (2 cases) and nonthyroidal illness(9 cases).[12]

Shyjing Ji et al also found11 thyroid dysfunction among treatment naïve HIV positive patients. Overall 18/74(24.3%) patients had thyroid dysfunction , among these 3(4.1%)patients had subclinical hypothyroidism, 12(16.2 %) had overt hypothyroidism , 3(4.1%) had hypothyroidism.

In our study, it was observed that age and gender had no significant association with the presence of thyroid dysfunction having p-value 0.165 and 0.654 respectively. It was noticed that duration of HIV was significantly associated with the presence of thyroid dysfunction with p-value 0.001 same as that found in the study done by

CONCLUSION

Our research revealed that thyroid dysfunction was significantly associated with treatment naïve patients of HIV. Age and gender had no significant association with the presence of thyroid dysfunction but duration of HIV was again significantly associated with the presence of thyroid dysfunction. It is therefore suggested that screening and/or monitoring of thyroid hormone in HIV-infected patients should be considered for timely intervention.

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TO EVALUATE THE DIAGNOSTIC ACCURACY OF FINE NEEDLE ASPIRATION CYTOLOGY IN THE DIAGNOSIS OF HEAD AND NECK MASSES BY TAKING HISTOPATHOLOGY AS GOLD STANDARD

Hamna Salahuddin, Sadaf Noor, *Muhammad Akhtar, *Muhammad Imran, Muhammad Oneeb Saleemi

Department of Pathology ,Sheikh Zayed Hospital Lahore

**PGR, *Assistant Professor, Allama Iqbal Medical College, Lahore*

Abstract

Background: Fine needle aspiration cytology (FNAC) is a simple, quick, non invasive and cost-effective method to sample superficial masses found in the Head and neck (H&N) region. It is also used as the main initial diagnostic investigation for lumps in the H&N region.

Objective: To evaluate the diagnostic accuracy of fine needle aspiration cytology in the diagnosis of head and neck masses by taking histopathology as gold standard

Material and methods: This was a comparative, cross sectional, study of 260 cases. FNAC and subsequent histopathological examination was done on head and neck swellings over a period of 6 months in local population of Punjab. Comparison of histopathological findings was performed with FNAC. Measures of validity i.e. Sensitivity specificity and accuracy of FNAC were calculated.

Results: A total of 260 FNACs were performed on patients presenting with head and neck lumps. Peak incidence of H&N lumps (36.5%) was noted in 51-60 years age group. Male to female ratio was approximately 1.3:1. The largest number of aspirates in this study were from cervical lymph nodes, 143(55%), followed by thyroid lumps 69(26.5%). Histopathological correlation was present in all the cases. Of these 260 cases, histological findings consistent with the cytological diagnoses were seen in 258(99.2%) cases and inconsistent findings in 2(0.77%) cases. The overall accuracy rate, sensitivity and specificity for H&N swellings, was 99.2%, 98.1% and 100%

Keywords: head and neck, FNAC, aspirates, lump

Head and neck (H&N) masses are one of the common presentations in patients referred for fine-needle aspiration cytology (FNAC) in pathology department. H&N masses include skin and adnexal swellings, thyroid nodules (TN) and swellings, nasal masses, paragangliomas, carotid body tumors, cervical lymphadenopathy, congenital cysts, masses in oral cavity and salivary gland enlargement.

FNAC is a simple, quick, and cost-effective method to sample superficial masses found in the H&N.[1] FNAC is used as the main initial diagnostic investigation for lumps in the H&N region.[2,3] Due to its minimally invasive nature, FNA possesses some advantages over biopsy.[4-7] No expensive instruments are needed.[8] This procedure is relatively safe, easy to perform and causes little discomfort to the patients.[9] Ancillary techniques such as flow cytometry, cytogenetics, electron microscopy and cell block preparations with immunocytochemistry can be applied for the characterization of tumors. In addition, their benefits include the lack of sedation or general anesthesia.[10] Moreover, it can be easily repeated in the event of non-diagnostic results, thus improving diagnostic precision.[11]

It is also used as initial screening test for thyroid follicular neoplasms.[17] The sensitivity and specificity of thyroid FNAC results have been reported as 65–99% and 72–100%, respectively. However, the

false-positive rate of FNAC results in thyroid cancer has been reported as 2–10%.[13-15] FNAC for non-thyroidal neck masses also has equal diagnostic yield to open biopsy.[16] A study conducted in Japan on 44 patients, the sensitivity, specificity and accuracy of FNAC for salivary gland was 42.9%, 100% , and 89.2%.[17] The usefulness of salivary gland FNA relates to the fact that it is easy to perform, is minimally invasive, smear evaluation is immediate, and the procedure can be repeated several times to obtain more tissue for diagnosis or special studies.[18]

METHODS

It is a comparative, cross sectional survey. Sample size of 260 cases is calculated using 95% confidence level, taking the expected frequency of head and neck lumps as (55%)5, with a margin of error of 5% for expected sensitivity as (89%)7 and a margin of error of 3% for expected specificity as (96%)7. It is a non probability, purposive sampling.

DATA COLLECTION 260 cases of H&N swellings taken, confidentiality of data was ensured. FNAC was done by using 5cc syringe. Smears were fixed with 95% ether alcohol solution. H&E was used. After FNAC, patients with resectable pathologies were referred for surgery. Excised specimens were evaluated by histopathological examination. Specimens were processed in automated tissue processor and H&E stain was used. Comparison of histopathological findings was performed with FNAC. Sensitivity specificity, accuracy of FNAC is calculated

RESULTS

The data was entered into SPSS version 17.0 and analyzed by using its statistical package

Sensitivity:

Sensitivity of FNA for H&N swellings is 98.13% with confidence interval (CI) of 93.41%-99.77%. Sensitivity of FNA according to regional distribution of H&N region is as follows:

For cervical lymadenopathies-98.39% (CI of 91.34% -99.96%),

For Thyroid lumps-95.65% (CI of 78.05%-99.89%),

For salivary gland swelings-100% (CI of 83.89%-100%)

Specificity:

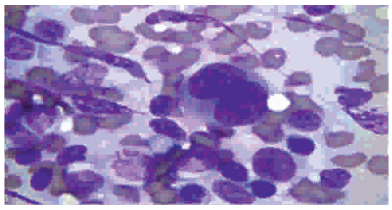
Specificity of FNA for H&N swellings is 100% with CI of 97.62%-100%. Specificity of FNA according to regional distribution is as follows:

For cervical lymphadenopathies-100% (CI of 95.55%-100%),

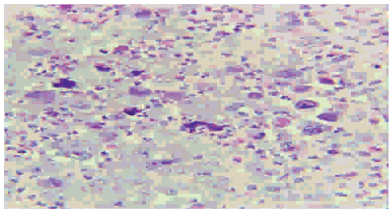
For thyroid lumps- 100% (CI of 92.29%-100%),

For salivary gland swellings-100% (CI of 86.77%-100%).

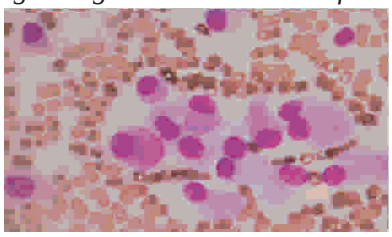
Accuracy :



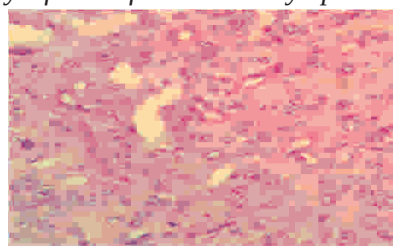
Accuracy of FNA for H&N swellings is 99.2%.



According to regional distribution of H&N region,



accuracy of FNA for cervical lymphadenopathies,



Thyroid lumps and salivary gland swellings is

99.3%,98.5% and 100% respectively.

a. Hodgkins lymphoma (cytology, 40x)

b. Hodgkin Lymphoma(Histology, 20x)

c. Medullary Carcinoma (Cytology, 40x)

d. Medullary Carcinoma (Histology, 40x)

DISCUSSION

The largest number of aspirates from H&N swellings in our study were from lymph nodes i.e. 143(55%), followed by thyroid lesions 69(26.7%), while the rest of the sites constituted 48(18.3%) cases. In the study by, Maniyar U and Amit,et al.[19], Maximum numbers of aspirates were also from lymph nodes (56.37%) followed by soft tissue lesions 14.80% whereas salivary gland, thyroid gland and miscellaneous lesions accounted for 11.44%, 10.90% and 6.49% respectively. The peak incidence of H&N mass lesions in this study was between 50 to 60 years (36.5%) of age group. Similar age group was also involved in the study conducted by Maniyar U, et al.[19] while the studies conducted by Setal C,et al.[20] and Khetrapal S, et al.[21] showed the peak incidence of H&N swelling between 21-30 years. Patel DN, et al.[22] conducted a similar study on 250 patients in India and found the peak incidence of H&N swellings between 31-40 year age group. This shows the variation in age range of patients presenting with H&N neck masses

The present study shows a slightly higher number of lesions in males i.e. 148(56.9%) than in females i.e. 112(43%). These findings were similar to the study conducted by Patel DN, et al[22] also found male predelication in his study, i.e. 52% male and 48% females, while studies conducted by Khetrapal S, et al.[21] Fernades H, et al.22and Vijay Tilak, et al.[23] found higher number of lesions in females.

Among the causes of cervical lymphadenopathy, malignancy was the most cause of Lymphadenopathy i.e. 61 cases (42.7%) followed by reactive lymph node enlargement, 43 cases(30%) and granulomatous lymphadenitis, 39 cases (27.3%). Similar results were seen in study conducted by Cheng AT and Dorman B24 where 50% cases were malignant in study by El Hag,et al.[25]

Among benign thyroid lesions, colloid goiter (comprising 26 cases,38%) was the most common pathology. 8(11.6%) cases of thyroiditis, 1(1.4%) case of hyperplastic change and 13(17.4%) cases of follicular adenoma were the other benign thyroid etiologies. Rout K, et al.[26] aspirated thyroid swellings in 76 patients in India and also found colloid goiter as the most common etiology of benign thyroid swelling. Similar results were seen in study conducted by Khetrapal S, et al.[21] Among the malignant causes of thyroid swellings, papillary carcinoma was the most common pathology i.e.12 cases (17.4%). Follicular carcinoma, medullary carcinoma and anaplastic carcinoma comprised of 6 (9%), 1 (1.5%) and 2 (3%) cases.

Out of a total of 69 cases of thyroid FNAC 68 cases showed consistent findings on histopathology and 1 case was found to be inconsistent on comparing cyto-histological features.

Histopathological correlation was present in all 47 cases of salivary gland swelling and cyto-histopathological findings were consistent in all the cases. Fernandes et al also noted a diagnostic accuracy of 100% among salivary gland lesions in their study.[27]

This study also included one case of skin and adenexal mass. The patient was a known case of carcinoma breast and presented with nodule on neck. FNAC showed metastatic mammary carcinoma, confirmed on histology.

The overall accuracy rate, sensitivity, specificity (99.2%, 98.1%, 100%,) for H&N swellings, calculated in our study, are high and well-accepted values for a diagnostic tool. These values are within the ranges quoted in the literature.[28-29,7] The specificity according to the literature ranges from 90% to 100%, sensitivity 81–94.2%, PPV 94–100%, NPV 81.25–94%, diagnostic rate 66–95% and accuracy rate 90–95.4%. These findings are also comparable with those of Fernandes H, et al.[27] who reported an overall diagnostic accuracy of 96.7% with specificity of 100% and sensitivity of 87.5%.[6] The high specificity (100%) of all the neck masses demonstrated in our study emphasizes the high efficacy of the utility of FNAC to identify negative results.

CONCLUSION

An almost perfect agreement between the cytological and histological findings with a sensitivity of 97.22% and specificity of 100%, for H&N swellings, was evaluated in this study. Hence, we conclude that FNAC is an excellent preliminary test and a useful adjunct to histopathology.

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FREQUENCY OF METABOLIC SYNDROME IN PATIENTS OF PSORIASIS

Nadia Ali Azfar, Lamees Mahmood Malik, Ikram Ullah Khan, Uzma Ahsan, Tariq Rashid, Muhammad Jahangir

Department of Dermatology, Allama Iqbal Medical College/Jinnah Hospital, Lahore.

Abstract

Background: Psoriasis is a common disorder affecting 1 to 3% of the world's population. Moderate to severe psoriasis has been associated with co - morbidities like metabolic syndrome which can be a cause of cardiovascular disease. Limited data is available regarding the frequency of metabolic syndrome in psoriatic patients in our population.

Objective: To determine the frequency of metabolic syndrome in patients of psoriasis and correlate it with the disease severity

Materials and Methods: A cross-sectional study was carried out in the Department of Dermatology, Jinnah Hospital Lahore, for a period of 6 months from March to September 2015. A total of 58 patients included in the study were suffering from any type and various grades of severity of psoriasis. They belonged to both genders and ages were between 15 and 70 years. The patients were examined clinically and severity of the disease was determined by PASI score. All cases were investigated for metabolic syndrome according to the criteria of National Cholesterol Education Program Adult Treatment Panel III. A control group of thirty-five age and sex matched patients suffering from chronic dermatoses other than psoriasis was also included. The findings were recorded on a pre-designed proforma.

Results: Out of the total 58 patients included in the study, 41 were males and 17 were females. Mean age was 36 + 2 years. Metabolic syndrome was present in 21 patients of psoriasis(36.2%) while in the control group, 5 out of 35 (14.29%) patients had metabolic syndrome.(p=0.061). Stratification of data on basis of disease duration and severity did not show any correlation with duration and severity of disease.

Conclusion: Patients of psoriasis have a higher incidence of metabolic syndrome than controls (p >0.05)

Key Words: Psoriasis, Metabolic Syndrome, PASI

Psoriasis is a common, chronic inflammatory skin disorder which affects people worldwide.[1] Metabolic syndrome is a combination of features which includes abdominal obesity, impaired glucose regulation, hypertriglyceridemia, low HDL cholesterol and hypertension.[2] Due to its chronic inflammatory nature it is thought that patients suffering from psoriasis are also prone to conditions having an inflammatory component i.e. cardiovascular disease and metabolic syndrome.[3]

Although it has been observed that psoriatic patients have an increased frequency of developing such problems, limited data is available regarding psoriasis and metabolic syndrome in our population. In this study we have tried to establish the association between the two conditions. This can help in better choice of drug therapy for treating psoriatic patients by keeping in mind the associations and side effects of medicines used for psoriasis. Early detection of metabolic syndrome in such patients may also help in reducing the morbidity and result in improvement of the quality of life of the patient.

METHODS

This descriptive, cross-sectional study was carried out in the dermatology department, Jinnah Hospital Lahore, Pakistan, from March to September 2015. A total of 58 patients of both genders, affected by psoriasis were enrolled from the inpa-

Correspondence: Dr. Nadia Ali Azfar, Associate Professor, Dermatology Dept, FJMU/SGRH

tient and outpatient departments. Patients on systemic steroids, retinoids and immunosuppressant therapy, known cases of diabetes mellitus, cardiovascular disease, pregnant / postmenopausal females and patients on oral contraceptive pills for last 6 months were excluded. The study was approved by the ethical review board of the hospital. A written informed consent was taken from all patients. The diagnosis was confirmed clinically. Severity of Psoriasis was graded according to the PASI score (Psoriasis Area and Severity index Score) as mild < 7, moderate 7-10, severe > 10. All cases were investigated for metabolic syndrome according to the criteria of National Cholesterol Education Program Adult Treatment Panel III. (Table.1) Three or more criteria are required for diagnosis. An age and sex matched control group of thirty-five patients suffering from chronic eczema was also investigated for metabolic syndrome. All findings were recorded on a pre-designed proforma and later analyzed.

RESULTS

A total of 58 patients were enrolled in the study. There were 41 males (70.69%) and 17 females. (29.31%) with a male: female ratio of 7:3. The ages ranged from 15 to 70 years. Mean age was 36 (SD + 2). The majority of patients (29.3%) belonged to the age group of 31- 40 years. Regarding the type of psoriasis, 51 (88%) patients were suffering from chronic plaque psoriasis, three each from pustular and erythrodermic psoriasis and only one patient suffered.

Metabolic syndrome was seen in 21(36.2%) patients of psoriasis. Ten patients out of these 21 (47.62%) were suffering from severe psoriasis (PASI more than 10) while 6 (28.57%) had moderate psoriasis. In the control group metabolic syndrome was seen in 5 patients (14.3%). The difference between the two groups was statistically significant (p = 0.016). Stratification of data on basis of disease duration and severity did not show any correlation with duration and severity of disease. (Table2 and 3)

DISCUSSION

Psoriasis is a chronic inflammatory skin disorder in which pro-inflammatory cytokines including IL-6 and TNF-α increase both locally and systematically.[1] It is thought that chronic inflammation results in metabolic diseases and pro-inflammatory cytokines give rise to the development of atherosclerosis, peripheral insulin resistance, hypertension, and type 2 diabetes thus giving rise to metabolic syndrome.[3]

This study reveals that metabolic syndrome is significantly more common in psoriasis patients than controls Recent studies showed that psoriasis is associated with metabolic disorders such as hypertension, type II DM, dyslipidemia, abdominal obesity, insulin resistance, and cardiac disorders and the risk of metabolic syndrome is increased in patients with psoriasis.[4] Other studies have also shown an increased frequency of ischemic heart disease, DM, hypertension, and dyslipidemia in patients with psoriasis when compared to controls.[5] Gisondi et al. found increased prevalence of hypertriglyceridemia and MS in psoriasis patients compared to controls.[6] Farshchian et al. however did not find any difference between psoriasis patients and controls in terms of fasting blood glucose, triglyceride, cholesterol and lipid levels.[7] In another study by Khan et al in Lahore it was observed that psoriasis is associated with smoking, DM, hypertension, and metabolic syndrome.[8]

Various studies have shown that metabolic syndrome was more prevalent in women.[9] When we stratified our results on the basis of gender we found no significant differences between male and female patients. Similarly, there was no correlation with age and the presence of metabolic syndrome in our patients. However Nisa and Qazi observed the higher prevalence of metabolic syndrome in psoriasis patients in the age group 18–30 years.[10]

There are controversies in the literature about the association of metabolic syndrome with severity of the disease. Sommer et al. reported a positive relation with severity, while Gisondi et al. and Nisa and Qazi found no relationship.[4,6,10] We also did not

observe an association between severity of the disease and metabolic syndrome.

It was reported that metabolic syndrome is related to the duration of the disease. Psoriasis starts in young ages in metabolic syndrome patients and duration of the disease is longer in patients with metabolic syndrome.[4,6,10] However we did not observe any correlation between disease duration and metabolic syndrome.

Limitations of our study were that it was a cross sectional study which does not enable us to observe the onset and evolution of the relationship of psoriasis with metabolic syndrome.

Our results showed that psoriasis predisposes to the development of metabolic syndrome. The present study was unable to confirm any relationship between the duration and severity of psoriasis and metabolic syndrome. A multidisciplinary approach is essential to reduce the co-morbidities and avoid serious complications in psoriatic patients. Therefore, we recommend evaluating psoriasis patients for the presence of metabolic diseases which may help in earlier diagnosis and start of management.

Table 1: *National Cholesterol Education Program Adult Treatment Panel III.*

Abnormality	Out-of-Range Values
Abdominal obesity	Waist circumference
	>102cm (>40in) males
	>88cm (35in) females
Impaired glucose regulation	Fasting glucose>5.55mmol/L
Hypertriglyceridemia	Triglycerides>1.69mmol/L
Low HDL-C	<1.03mmol/L males
	<1.29mmol/L females
Hypertension	> 130/85mmHg either
	systolic or diastolic

Table 2: *Correlation of Metabolic Syndrome with Disease Duration*

Duration of psoriasis	Metabolic syndrome		p value
	Yes	No	
< 1 yr	6	10	X^2= 1.055
1-5 yr	8	10	p = 0.590
>5 yr	7	17	
Total (n=58)	21	37	

Table 3: *Correlation of Metabolic Syndrome with Disease severity*

Severity of Psoriasis	Metabolic syndrome		p value
	Yes	No	
Mild	5	12	X^2= 0.931
moderate	6	12	p = 0.628
severe	10	13	
Total (n =58)	21	37	

Tables and Figures:

CONCLUSION

Patients of psoriasis have a higher incidence of metabolic syndrome as compared to controls.

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TO DETERMINE THE EFFICACY OF SMALL-BORE THORACIC CATHETER IN THE MANAGEMENT OF SECONDARY SPONTANEOUS PNEUMOTHORAX

Salman Ayyaz[1], Muhammad Rauf[2], Afshan Qureshi[3], Asif Hanif[4], Rashmi Giri[5], Muhammad Saqib Saeed[6]

[1]Associate Professor, Pulmonology, KEMU, Mayo Hospital Lahore; [2]Assistant Professor, Pulmonology, QAMC, Bahawal Victoria Hospital, Bahawalpur; [3]Assistant Professor, Radiology, KEMU, Mayo Hospital, Lahore; [4]Assistant Professor, Pulmonology, KEMU, Mayo Hospital, Lahore; [5]Post Graduate Resident, Pulmonology, KEMU, Lahore; [6]Professor, Pulmonology, KEMU, Mayo Hospital, Lahore;

Abstract

Our study focused on the efficacy of Small bore thoracic catheter in the management of Secondary Spontaneous Pneumothorax, as there is lack of widely accepted management guidelines for this important clinical condition.

Material and Methods: Thirty eight(38) patients were included in the study as per inclusion criteria. Different cases of secondary pneumothoraces caused by Chronic Obstructive Pulmonary Disease, Asthma COPD overlap syndrome, Tuberculosis, Interstitial lung disease, Pneumonia as well as Iatrogenic cases were included in the study. The duration of study was 6 months spanning from March to September 2018. The primary endpoint was complete or nearly complete lung expansion on clinical examination and chest x-ray following Small bore thoracic catheter insertion. The secondary endpoint was no recurrence of pneumothorax at 1 and 3 months follow-up after extubation.

Results: Thirty(30) patients were successfully treated as per the primary and secondary end points while eight(8) patients had failure. Failure was due to minor complications like kinking/malposition in two(2) patients, dislodgement in one(1) patient and subcutaneous emphysema secondary to disease related large Broncho-pleural fistula(BPF) in five(5) patients. No mortality or any major complications like massive bleeding, shock or tension pneumothorax was observed.

Conclusion: Using the SBTC is an effective, feasible and minimally invasive approach for the treatment of secondary spontaneous pneumothorax. Although, further studies on larger patient groups are required to confirm our findings.

Keywords: Secondary spontaneous pneumothorax(SSP), small-bore thoracic catheter(SBTC), Large chest tube(CT)(16-22F),Asthma COPD overlap Syndrome(ACOS), Broncho-pleural fistula(BPF).

OBJECTIVE: Study was conducted to determine the efficacy of small bore thoracic catheter in the management of secondary spontaneous pneumothoraces.

The term 'pneumothorax' which refers to abnormal presence of air in the pleural cavity was first coined in 1803 when most cases of pneumothorax were secondary to Tuberculosis. The classification of pneumothorax was endured by Kjærgaard in 1932 with the first modern description of pneumothorax occurring in healthy people and is known as Primary spontaneous pneumothorax. In distinction to Primary spontaneous pneumothorax, Secondary spontaneous pneumothorax is associated with underlying lung disease and instead of Tuberculosis, COPD is now the commonest underlying lung disease causing SSP(1). The consequences of a pneumothorax in patients with pre-existing lung disease are significantly greater, and at times becomes potentially life-threatening if there occurs

Correspondence: ayyazsalman@yahoo.com

undue delay in the prompt management.

For Primary Spontaneous Pneumothorax, the BTS recommends simple observation for small pneumothoraces (<2 cm, BTS). For large Primary Spontaneous Pneumothoraces (>2 cm) either symptomatic or asymptomatic, simple aspiration is recommended as the first-line treatment and SBTC drainage subsequently as required.

For SSP, the BTS recommends the insertion of SBTC (≤14F catheter),[1] whereas the ACCP consensus conference recommended a larger chest tube (CT) (16-22F catheter).[2]

A recent survey showed drainage via a large CT was still very common for the management of Primary Spontaneous Pneumothorax, and only half of physicians used a small-bore thoracic catheter. However, in secondary spontaneous pneumothorax (SSP), there is lack of widely accepted management guidelines. The continued progress of guidelines favor towards less invasive management with the use of smaller catheters, which are easier and faster to insert with less patient discomfort and complications.[3]

Our study focused on the efficacy of SBTC in the management of secondary pneumothorax. Different cases of secondary spontaneous pneumothoraces caused by COPD/ACOS, Tuberculosis, ILD (interstitial lung disease), Pneumonia as well as Iatrogenic cases were included in the study.

METHODS

All patients were admitted in Institute of TB and Chest Medicine, Mayo Hospital, Lahore. Thirty eight (38) patients were included in the study which consisted of twenty eight (28) male and ten (10) female with a mean age of 45. The duration of study was 6 months spanning from March to September 2018.Different aetiologies of secondary pneumothoraces were managed using a small-bore thoracic catheter and analyzed.

Inclusion criteria:

(i) Age > 13 years

(ii) Secondary spontaneous pneumothorax (SSP)

(iii) first episode of SSP

(iv) Iatrogenic

Exclusion criteria:

(I) Hydropneumothorax

(ii) Pyopneumothorax

(iii) Recurrent pneumothorax

(iv) Tension pneumothorax

(v) Traumatic pneumothorax

Treatment Protocol

SBTC was inserted regardless of the cause of secondary pneumothorax. Easy drains (SBTC/ Vygon) of ≤10F were used. After skin disinfection and field preparation, a needle was introduced into the intercostal space under local anesthesia. Blade (no.11) was used for a small incision if required, especially in obese patients. After the needle entered the pleural space, it was directed apically and the catheter present inside the needle was advanced into the pleural space. The catheter was fixed to the skin using suture/silk and sterile adhesive tape .

The inserted catheter(≤10F) was connected via a three-way valve to a 50-ml syringe and air was manually aspirated to confirm the correct placement of catheter inside the hemi-thorax and was later re-confirmed on chest x-ray(CXR)

The catheter was then connected to under water-sealed bottle. Negative suction of (-10 to -20 cm H_2O) was applied on all the cases for the initial period of 24 to 48 hours. Lung expansion was assessed periodically by clinical examination and chest x-ray. The catheter was then removed after ensuring that there was no air leakage or bubbling from the chest tube system.

The primary endpoint was defined as complete or nearly complete lung expansion on chest x-ray following SBTC insertion without any residual air leak and/or the need for a large CT or surgical treatment.

The secondary endpoint was no recurrence of pneumothorax at 1 and 3 months follow-up after extubation.

Data was entered and analysed in SPSS V.26. Qualitative variables like gender and different diseases causing SSP were represented in frequencies and percentages while quantitative data like age was presented in mean ±standard deviation.

RESULTS

Thirty eight (38) patients with mean age of 45±5 were included in the study. Twenty eight (28) were male and ten (10) were female. Among them, nineteen (19) were secondary to COPD/ACOS, five (5) were due to Bronchiectasis , four (4)were ILD (NSIP), four (4) were Tuberculosis, one (1) was PCP(Pneumocystis carinii pneumonia), one (1) was secondary to Langerhans Cell Histiocytosis (LCH) and four (4) were Iatrogenic cases. There were no mortalities or any major complications like massive bleeding, shock, or tension pneumothorax in any case. Thirty (30) patients were successfully treated and met the primary and secondary end points while eight (8) patients had failure (Table 2). Failure was due to minor complications like kinking/malposition in two (2) patients, dislodgement in one (1) patient and subcutaneous emphysema secondary to disease related large BPF in five (5) patients. (Table 3)

Table 3: *Reason for failure*

DISCUSSION :

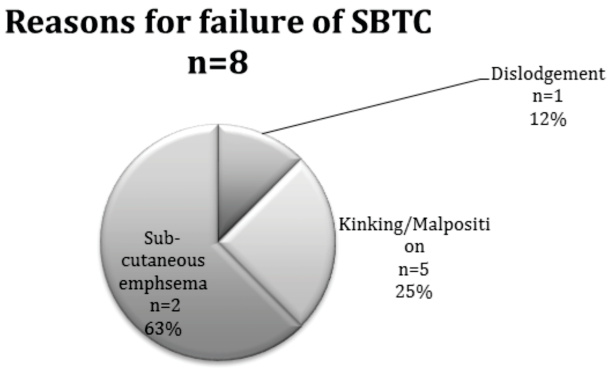
Table 1: *Characteristics and Causes of Secondary Pneumothorax*

	n=38	Percentage
Age, years	45± 5	
Gender	m=28	73%
	f=10	27%
COPD	19	50%
Bronchiectasis	5	13.1%
ILD(NSIP)	4	11%
Tuberculosis	4	11%
PCP	1	2.7%
Langerhans Cell istiocytosis(LCH)	1	2.7%
Iatrogenic	4	11%

Table 2: *Outcome of SBTC*

	Success	Failure
COPD/ACOS	15	4(21%)
Bronchiectasis	4	1(20%)
ILD(NSIP)	3	1 (25%)
Tuberculosis	2	2 (50%)
PCP	1	0
Langerhans Cell istiocytosis(LCH)	1	0
Iatrogeic	4	0
Total	30	8 (21%)

This study focused on the efficacy of SBTC for



the management of Secondary Spontaneous Pneumothoraces as well as Iatrogenic cases. There is lack of widely accepted management guidelines for SSP yet. In this study, we found that SBTC drainage was fully effective in the initial management of secondary spontaneous pneumothoraces, irrespective of its cause. Iatrogenic cases were also included in the study and though no. was small (i.e. four cases), all the cases were successfully treated in this sub-group. Negative suction of (-10 to -20 cm H2O) was applied on all the cases for the initial period of 24 to 48 hours. The insertion of a SBTC into the pleural space is easier, safer, faster to implement and associated with less pain and discomfort than large CT insertion. SBTC drainage appears as effective as conventional Chest tube drainage, and results in a smaller scar after removal of the catheter. Rate of major complications i.e. bleeding, shock, tension pneumothorax were negligible and duration of hospital stay was also shortened with the use of SBTC. There were no mortalities or any major complications like massive bleeding, shock or tension pneumothorax.

The reasons for failure of SBTC in 8 cases were sorted out and corrected. There were five(5) cases of

sub-cutaneous emphysema secondary to disease related large BPF. Two(2) of them were due to Tuberculosis, two(2) cases were due to COPD/ ACOS and one(1) case was due to ILD. All these cases were initially treated with the application of negative suction(-15 to -20cm H20) on SBTC for period of 48 to 72 hours. Later, large CT was inserted for their subsequent management. Though only 4 patients of Tuberculosis were included in the study, the failure rate due to BPF was high in this sub-group i.e. 2 out of 4 (50%).

A few small and non-comparative studies have demonstrated the safety and effectiveness of small-bore thoracic catheters in patients having first episodes of spontaneous (4-12) or iatrogenic pneumothoraces.[5-7,10,13-16] These results were supported by 4 retrospective comparative studies that found that small-bore catheters (8-14F catheter) were as effective as large CTs in treating spontaneous pneumothoraces,[17-20] whether primary[17,18,19] or secondary.[18,19,20] In these previous studies, SBTC were used in 50 Primary Spontaneous Pneumothorax[17] and 69 SSPs.[20] Consistent with the recent BTS guidelines[(1)], our study supported that large CT drainage should not be used as the first-line approach in SSP management.

Therefore, in our setting we no longer use large CT in the initial management of SSP, and a small bore thoracic catheter is preferred as the first line mamagement, whether the cause of spontaneous pneumothorax is Primary or Secondary.

CONCLUSION

In conclusion, using the SBTC is an effective, feasible and minimally invasive approach for the treatment of secondary spontaneous pneumothorax. Although, further studies on larger patient groups are required to confirm our findings.

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EFFICACY OF 0.03% TACROLIMUS OINTMENT VS 1% HYDROCORTISONE ACETATE CREAM IN CHILDREN WITH MILD TO MODERATE ATOPIC DERMATITIS

Naima Aliya, Lamees Mahmood Malik, Nadia Ali Azfar, Sehrish Rashid, Khadija Malik, Shaista Umbreen, Tariq Rashid

Department of Dermatology Unit 1, Jinnah Hospital Lahore

Abstract

Objective: To compare efficacy of 0.03% tacrolimus ointment versus 1% hydrocortisone acetate cream in children with mild to moderate atopic dermatitis.

Methods: This study was carried out in department of dermatology, unit 1, Jinnah hospital, Lahore. A total of 140 patients with mild to moderate atopic dermatitis (70 patients in each group) were included in the study. In group A, patients received 0.03% tacrolimus ointment twice daily for 3 consecutive weeks and in group B, 1% hydrocortisone acetate cream twice daily for 3 consecutive weeks was applied.

Results: Efficacy was seen in 49 patients (70.0%) of group A and 35 patients (50.0%) of group B. There was a statistically significant difference between two groups (p=0.016). Efficacy was graded as excellent and good. In group A, excellent grade was seen in 9 patients (12.8%) and good grade in 40 patients (57.2%). While in group B efficacy grade was excellent in 8 patients (11.4%) and good in 27 patients (38.6%).

Conclusion: Tacrolimus 0.03% ointment was significantly more effective than 1% Hydrocortisone acetate cream (p=0.016) in the treatment of mild to moderate atopic dermatitis in children.

Key Words: Atopic dermatitis, Tacrolimus ointment, Hydrocortisone acetate cream, Efficacy.

Atopic dermatitis is a chronic relapsing inflammatory skin disease, characterized by itchy papules which become excoriated and lichenified and typically have a flexural distribution.[1] Majority of the patients have a personal or family history of "atopic diathesis" and have intermittent flares and symptom-free periods.[2] Atopic dermatitis is a genetically complex disease with impaired skin barrier and variety of defects in innate immunity that affect the development and severity of atopic dermatitis.[3,4] The severity has some positive correlation with the absolute eosinophil count and serum IgE levels.[1]

Atopic dermatitis affects up to 20% of children worldwide and can persist into adulthood.[3,4] It has a significant impact on the quality of life of patients and their families and also marked economic impact[3]. Patients have low self esteem and sometimes cannot enjoy social interactions. Growth and height of the affected children is also compromised [1].

Topical corticosteroids form the mainstay of treatment and, along with emollients, are able to control the condition in more than 80% of the cases. However, adverse effects of topical steroids limit their long-term use such as skin atrophy, acne, allergic contact dermatitis.[1,2] Children are especially more prone to the systemic adverse effects of topical steroids because their skin has poorly developed barrier function and a large surface area [5].

The use of maintenance steroid-sparing therapies is desirable which may prevent relapse and decrease the severity of disease.[2] Tacrolimus, an immunomodulator, has been found to be effective and safe alternative in the long term treatment of disease in pediatric and adult patients[1,6]. Intermittent application of 0.03% tacrolimus ointment offers a useful steroid-sparing approach to maintaining stabilization of atopic dermatitis.[2] Unlike corticosteroids, tacrolimus is not atrophogenic. [6]

However, its use is associated with few side effects. The most common adverse events are mild to moderate burning, erythema, pruritus, folliculitis and herpes simplex infections[5,6]. Topically, tacro-

limus has been used in 0.03% and 0.1% ointment. In pediatric patients aged 2 years and older, 0.03% is preferred, while in adults and geriatric patients 0.1% may be used 2 times a day.[6]

Few local studies are available which compared efficacy of tacrolimus and topical steroids. The present study was planned to compare the efficacy of these two treatment regimens with a view to find a more effective treatment with lesser side effects for a condition which may require long term treatment in the pediatric population.

METHODS

This study was carried out in outpatient department of dermatology unit 1, Jinnah Hospital, Lahore. A total of 140 patients between 2 – 14 years of age having mild to moderate atopic dermatitis with EASI score less than 52.8 were included in study. Patients who had taken any form of topical or oral medication in last 04 weeks prior to study, patients with acute herpes simplex infection and with secondary bacterial infection were excluded from the study. Written informed consent was taken from the parents. Patients were randomly allotted to Group A or B, 70 patients in each group. Baseline EASI score was calculated in all patients. In Group A, patients applied 0.03 % tacrolimus ointment twice daily, while group B patients applied 1 % hydrocortisone acetate cream twice daily for 03 consecutive weeks. Decrease in EASI score was noted at intervals of one week up to 3 weeks and final assessment regarding efficacy of treatment was made at the end of 3rd week. Efficacy was compared in both groups by using chi-square test taking p-value < 0.05 as significant. Efficacy was graded as excellent, good, satisfactory and poor on the basis of percentage reduction of EASI score from baseline.

RESULTS

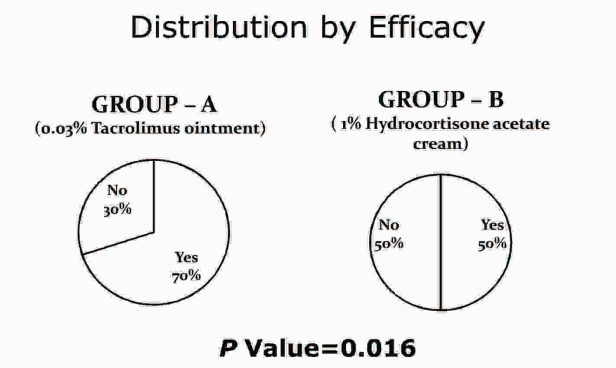
A total of 140 patients, 70 in each group were studied, mean age of patients was 7.56±3.14 and 8.09±2.94 years in group-A and B, respectively. In group-A male to female ratio was 0.65 : 0.34, while in group B male to female ratio was 0.58 : 0.41. Disease was of mild severity in 32 patients (45.7%) of group-A and 29 patients (41.4%) of group-B while disease was of moderate severity in 38 patients (54.3%) in group-A and 41 patients (58.6%) in group-B (Table 1). Efficacy was seen in 49 patients (70.0%) of Group-A and 35 patients (50.0%) of group-B (Figure 1). Statistically significant difference was found between the efficacy of two groups (p=0.016). Grades of efficacy were excellent in 9 patients (12.8%) of group-A and 8 patients (11.4%) of group-B and good in 40 patients (57.2%) of group-A and in 27 patients (38.6%) of group- B (Figure 2).

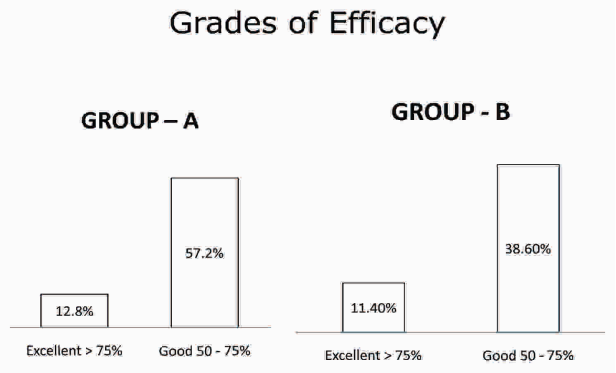
FIGURE 1

Table 1:

Mean age (years)	Gender		Severity	
	Male	Female	Mild	Moderate
	n (%)	n(%)	n(%)	n(%)
7.56± 3.14	46 (65.7 %)	24(34.3%)	32(45.7%)	38(54.3%)
8.09 ±2.94	41(58.6%)	29 (41.4%)	29 (41.4%)	41(58.6%)

FIGURE 2





DISCUSSION

Atopic dermatitis is a disease resulting from the

interaction of genetic, environmental and immunological factors and presents many clinical aspects[7]. Topical corticosteroids are used commonly to treat atopic dermatitis flares. However their long term use is associated with various adverse effects. These include skin atrophy, striae, telangiectasia, acne, glaucoma, adrenocortical insufficiency, and in extreme cases, Cushing syndrome[8]. However, there is no conclusive evidence that correctly used topical agents cause significant systemic side-effects[9]. In fact, literature suggests that when used for periods of up to four weeks, topical corticosteroids are safe and effective in treating atopic dermatitis flare-ups[9]. Conversely, it is the long-term use or overuse that is associated with adverse effects [9].

Earlier studies have demonstrated that tacrolimus ointment is effective for the treatment of atopic dermatitis[10]. Tacrolimus ointment is suitable for the short and intermittent long-term treatment of moderate to severe atopic dermatitis in patients over 24 months old who are not adequately responsive or are intolerant to conventional therapies, such as topical corticosteroids[7]. A significant improvement of the disease is noted within 1 week of starting tacrolimus therapy. For adult and pediatric patients, the ointment should be applied at the first sign of dry skin or pruritus[7]. Long term efficacy and safety are even more promising. Unlike potent corticosteroids, tacrolimus ointment can be used to reduce the incidence of disease flares and also the severity of flares without the risk of corticosteroid-related adverse events.[11]

In present study, majority of the children having atopic dermatitis were between 6-10 years of age with a mean age of 7.56 and 8.09 in groups A and B respectively. The gender of majority of patients in both groups was male i.e. 65.7% in group A and 58.6% in group B. The overall sex ratio was seen to be equal by previous researchers.[12] However a study done by Chian- Yaw et al in 2010 showed that the prevalence of atopic dermatitis in females was lower than that in males before the age of 8 years but became higher after that. As majority of our patients were between 6-10 years of age the male predominance found in our study is comparable with these results.[13]

In our study tacrolimus 0.03% ointment showed efficacy in 70% patients as compared to 50% patients treated with 1% hydrocortisone acetate cream. The difference between these two groups was statistically significant ($p< 0.05$). When we compared our results with previous studies, tacrolimus ointment was also reported by Reitamo et al in (2002), (2004), (2005) and Hofman (2006) as more efficacious than corticosteroids [14,15,16,17].

The limitation of the present study was its small sample size. Also we only used 0.03% tacrolimus ointment in our patients. Various studies show that tacrolimus 0.1% was significantly better compared to the 0.03% formulation (p-value < 0.05).[7]

Tacrolimus offers an alternative to the treatment of moderate-to-severe atopic dermatitis and steroid-resistant atopic dermatitis. It may be useful in treating atopic dermatitis at sensitive sites such as the face, where the use of potent topical steroids carries a high risk of skin thinning and telangiectasia[15]. Our study shows promise that application of 0.03% tacrolimus ointment offers a novel, steroid-sparing approach to maintaining stabilization of atopic dermatitis that seems both safe and efficacious.

CONCLUSION

In conclusion, Tacrolimus 0.03% ointment was significantly more effective than 1% hydrocortisone acetate ointment (p=0.016) in the treatment of mild to moderate atopic dermatitis in children.

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COMPARISON OF SERUM ADIPONECTIN LEVELS IN MIGRAINE PATIENTS AND CONTROLS

Maria Anwar[1], Javaria Latif[2], Tabinda Kazmi[3], Warda Anwar[4], Shumaila Dogar[5], Ambreen Anjum[6]

[1]Sheikh Zayed, Federal Post-Graduate Medical institute, Lahore, Amna Inayat Medical College, Lahore; [2]Shahida Islam Medical College; [3]Niazi Medical and Dental College, Sargodha; [4]Al-Aleem Medical College; [5]FMH Medical College; [6]Al Aleem Medical College.

Abstract

Background: Migraine is one of the commonest primary headache syndromes rated by WHO to be as disabling as quadriplegia, psychosis and dementia. Migraine is defined as a recurrent, incapacitating neurovascular disorder characterized by attacks of debilitating pain associated with photophobia, phonophobia, nausea and vomiting. Migraine has been seen to affect 16% of the general population. It has been found to be associated with increased levels of serum Adiponectin (ADP). There is no laboratory investigation to diagnose migraine. It is diagnosed on purely clinical basis. Raised levels of Adiponectin can associate it with migraine and it can make Adiponectin a candidate biomarker to diagnose the disease through simple laboratory investigation.

Objectives: The objective of this study was to compare serum adiponectin levels in migraine patients and healthy controls.

Design: It was cross sectional, comparative study.

Place and duration of study: The duration of study was six months, September 2015 – February 2016.It was conducted in Shaikh Zayed medical complex.

Material and method: Serum Adiponectin levels were measured and compared in 80 subjects divided in two groups, migraine group and a healthy control group.

Results: Mean serum Adiponectin levels of control group were (34.5 ± 9.2) ng/mL and mean serum Adiponectin levels in migraine group were (38.9 ± 10.1) ng/mL with a p-value of 0.042, which is statistically significant.

Conclusion: Measured ADP levels were raised in migraine group as compared to healthy controls.

Key words: Adiponectin, migraine

Migraine is the ubiquitous and widely occurring primary headache syndrome worldwide[1]. The prevalence of this headache is witnessed more in the age range of 25-55 years.[2] It was found that 16% of the world population is prey to distressing life due to migraine. Quality life assurance of migraineurs is perturbed and ruffled. A number of studies promulgated impact of migraine on physical, mental and social aspects of life to be deleterious when compared to healthy subjects.[3] Migraine attack period in diseased personages brings poor family relationships, abysmal and inadequate educational performance and student related activities.[4] World Health Organization (WH0) has classified this tormenting headache to be as crippling as other disorders like quadriplegia, psychosis and dementia.[5] Migraine is defined 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".[6]

The pathophysiology of this complex, agonizing and chronic, neurovascular disorder is still vague and cryptic but initiation and prolongation of pain is attributed to the episodic activation of the

trigeminal system; in particular, trigeminal ganglia.[7] The excitability of the brain changes during the attack of migraine and it leads to the increased excitation of trigeminovascular system (TVS) and vasodilation of brain vasculature.[8] The TVS innervate the cranial vasculature and dura matter. Certain areas of central nervous system like, areas of the brainstem (locus coeruleus and periaqueductal grey area), thalamus and hypothalamus are connected with the TVS via ascending connections to brain areas from TVS. These connections travel through trigeminothalamic and trigeminohypothalamic tracts. Different neuropeptides i.e. calcitonin gene related peptide, substance P, neurokinin A, vasoactive intestinal polypeptide, nitrous oxide and acetylcholine are released due to activation of these sensory afferents and leads to migraine pain and inflammation.[9,10,11] CGRP at physiological concentrations and possibly via stimulation of its selective receptors on T-cells, triggers the secretion of different cytokines like IL-6, iL-1, TNF alpha. IL-6 and Nuclear factor kappa β(NF-kβ) are increased during acute migraine attacks.[12,13] IL–6 contributes to proinflammatory signaling that eventually leads to increased blood vessel permeability, tissue edema of the brain tissues, and pain sensitization, this provides in part the molecular and functional mechanisms related to migraine pain in dura mater.[14]

Adiponectin is one of the adipokines predominantly produced by adipocytes (subcutaneous adipose tissues > visceral adipose tissue). It is cardinally involved in inflammation, metabolism of glucose and lipids, and energy homeostasis processes.[14] The discovery of adiponectin took place when human cDNA project expressed the genes of human adipose tissues.[15] The gene of adiponectin is located on chromosome 3q27 which is expressed in enormous amount.[16] Structurally, adiponectin has 244 amino acids, single peptide whose N-terminus has a domain similar to collagen and C-terminus has a globular domain.[17] Several types of Adiponectin receptors have been found in different organs of body. Most widely studied are adiponectin receptors 1(AdipoR1) and adiponectin receptor 2 (AdipoR2). They are present in hypothalamus, peri-aqueductal grey area and brainstem and hepatocytes.[18] Adiponectin has anti-inflammatory properties. It has protective role in those diseases which have inflammation in their pathophysiology.[19]

Adiponectin is associated with migraine centrally through migraine involved brain areas like hypothalamus. Receptors of adiponectin are expressed on anterior hypothalamus, posterior hypothalamus and paraventricular nucleus. Recording of positron emission tomography supports the activation of hypothalamus during migraine attack, so the key of connection may lie in altering of adiponectin receptors on hypothalamus in attack period.[20] Besides this central link of migraine with adiponectin, the two are also interrelated peripherally. Abnormalities in cytokine levels have been noted in the blood of migraine sufferers. Specifically, NF-κβ and the proinflammatory cytokines, TNF-α, IL-1β, and IL-6, have all been shown to be increased[13]. Adiponectin is connected to migraine in this way as it is also involved in the activation of proinflammatory nuclear factor kappa β (NF-κβ) pathways and it also stimulated release of nitric oxide, a potent vasodilator, the proinflammatory cytokines, IL-6 and TNF-α.[21]

The objective of our study was to compare serum levels of Adiponectin in migraine patients and controls. Elevated levels in diseased subjects will strengthen the association of adiponectin with migraine, a step further in labeling adiponectin as candidate biomarker. Because, despite widespread prevalence, migraine still lacks a diagnostic test to accurately label a patient as “migraineur”.

METHOD

It was a cross sectional, comparative study conducted in the department of Physiology, Shaikh Zayed Postgraduate Medical Institute, Lahore and Neurology department, Shaikh Zayed hospital, Lahore after taking permission from the respective head of departments. The study duration was six months.

A study population of 80 individuals was selected according to inclusion and exclusion criteria, and was categorized into two groups, as

follows:

Group A: This was the control group which included 40 healthy individuals, having no signs, symptoms or complaints of migraine. Healthy subjects were recruited from students and faculty of Shaikh Zayed Medical complex.

Group B: This group included 40 migraine patients. They were clinically diagnosed migraine patients 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:

Controls and migraine patients with other causes of headache i.e. tension headache and cluster headache.

Migraine patients were enrolled from the out-patient clinics of Neurology Department of Shaikh Zayed medical complex fulfilling the inclusion criteria. Controls were taken from faculty and students of Shaikh Zayed medical complex. After getting written informed consent, the demographic data of all the subjects was collected and every individual was assessed by taking history and using specially designed questionnaire. Blood samples were taken. Serum Adiponectin levels were estimated by using ELISA technique in Pathology Laboratory of Shaikh Zayed Medical Complex.

The data was entered into and analyzed by SPSS (Statistical Package for Social Sciences) version 20.0. Independent sample t-test was applied to compare the mean serum Adiponectin levels between both groups. p value less than 0.05 was considered statistically significant.

RESULTS

Following results were obtained:

DISCUSSION

In this research the levels of serum Adiponectin in age and BMI matched two comparative groups which included migraineurs who fulfilled the criteria of diagnosis for migraine, and a healthy control group were compared. Mean age of group A was 30.17.02 years and that of group B was28.7±6.8 years. BMI of Group A and Group B was 21.43 ±2.02kg/m^2 and 22.08±1.94kg/m^2 respectively.

The mean serum Adiponectin levels of group A was 34.5 ± 9.2ng/mL and mean serum Adiponectin levels of group B was 38.9 ± 10.1ng/mL. The data was normally distributed and independent sample t-test revealed that there was statistically significant difference in mean serum Adiponectin levels between both groups (p-value = 0.042). Serum Adiponectin levels were higher in patients of migraine but there was no equal rise in healthy control group.

Our raised levels were in line with another study conducted by Pterlin et al. It was the pioneer research program which compared the adiponectin levels between healthy controls and migraineurs. The value of serum adiponectin was calculated to be significantly higher (p\0.005) in migraineurs than controls, this study even found raised levels more pronounced ictaly[22].

Duarte et al. published the work which clearly found the statistically significant increased serum adiponectin levels in migraine population. The sample size of study was 130, among them 68 individuals were clinically diagnosed migraine patients and 65 were controls. They were age, gender and BMI matched and results showed elevated adiponectin levels in migraineurs[23]. Clara et al, also second this view by showing significantly raised adiponectin levels in migraineurs, it also showed correlation between adipocytokine levels and other inflammation related molecules[24]. Dearborn et al. also found higher Adiponectin levels in migraineurs.

Table 1: *Comparison of Serum ADP Levels (ng/mL) between both Groups*

	Serum ADP Levels (ng/ml)			
	Mean ± SD	**Minimum**	**Maximum**	**p- value**
Group A	34.5 ± 9.2	16	48	0.042*
Group B	38.9 ± 10.1	20	59	

* p-value is significant, independent sample t-test

Though this specific study found that there was interlinkage with the gender such that the elating levels of Adiponectin were associated with increased odds of migraine in older men, but not female population. That was attributed to the lower testosterone levels in older men.[25]

In contrast to this Lippi et al. gave contradictory reports as they failed to find raised adiponectin levels in migraine population when data was analyzed between migraine population and healthy controls.[26]

While the neoteric research advocates the link of adiponectin with migraine by addressing various aspects of disease pathophysiology. Scrupulous studies using assiduously constructed designs and methodology is needed to vigilantly consider pain state during sampling and its effects on adiponectin levels. We did not put a halt to preventive treatments during study which could have affected our results.

These limitations are recommended to be addressed in future research programs.

CONCLUSION

Though contemporary institutes are operational on this topic but quite a few data are obtained to reasonably label the proposed association. Our study would help in providing aid in this emerging concept of relating adiponectin with migraine. This study not only helps in finding a link between migraine and Adiponectin, it also brings Adiponectin in limelight as postulant, viable biomarker for migraine diagnosis.

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ENDOSCOPIC CLASSIFICATIONS OF GASTRITIDES AND GASTROPATHIES: A RETROSPECTIVE ANALYSIS CARRIED OUT AT LIVER CLINIC, LAHORE, PAKISTAN

Rana Muhammad Suhail Khan[a], Ghulam Mustafa[b], Rao Hashim Idrees[c], Muhammad Maqsood[c], Jamshad Latif [c], Aftab Mohsin[a]

[a]Allama Iqbal Medical College / Jinnah hospital, Lahore, Pakistan

[b]Department of Computure Sciences, Bahria University, Lahore, Pakistan

[c]Gujranwala Medical College/Teaching Hospital, Gujranwala, Pakistan

Abstract

Objective: To determine the prevalence of different subtypes of gastritides and gastropathies amongst patients who underwent upper GI endoscopies (UGIE) at Liver clinic, Lahore, Pakistan.

Study Design: Retrospective cohort study

Methodology: The patients who underwent UGIE from 1st July 2011 to 30th June 2014 were included. Mucosal erythema and edema without erosive changes defined acute non-erosive gastritis (ANG), where addition of erosions, ulcers, sub-epithelial hemorrhages and reddish streaks were named as acute erosive gastritis (AEG). Thin pale shiny mucosa with prominent subepithelial vasculatures, and cobblestone appearance due to mucosal nodularity defined the chronic atrophic gastritis and chronic nodular gastritis respectively. In liver cirrhosis patients, mosaic-like pattern of gastric mucosa was named as PH. Similarly other subtypes were also named based on morphology. The entire data was evaluated on SPSS version 25. During descriptive interpretation of data, means and standard deviations were calculated for quantitative variable, and frequencies and percentages for qualitative variables.

Results: Out of the total of 3456 patients, 92.6% patients had endoscopic features suggestive of gastritis and gastropathies. 60.8% were male and 39.2% were female. Their mean age was 48.54 + 12.96 years and mean weight wa 71.80 + 16.2 Kilogram. Amongst 1070 gastritis patients, 51.8% had acute non-erosive gastritis, 37.2% reactive gastropathy (acute erosive gastritis), 6.2% nodular gastritis and 4.7% atrophic gastritis. Amongst 2404 gastropathy patients, 98.98% had portal hypertyensive gastropathy, 0.93% prolapse gastropathy and 0.09% hyperplastic gastropathy. Amongst patients with reactive gastropathy, dominant gastric findings suggestive of the diagnosis were erosions (53.8%, n=188), linear antral reddish streaks (39.5%, n=138), subepithelial hemorrhages (2.8%, n=10) and multiple gastric ulcers (3.7%, n=13).

Conclusion: Portal hypertensive gastropathy was the commonest gastric finding in upper gastrointestinal endoscopies amongst our patients. This reflects the high burden of liver cirrhosis in our country. Other gastropathies like prolapse and hyperplastic were seen in a very little proportion of the patients. Acute non-erosive gastritis was the commonest type of gastritis followed by acute erosive, chronic nodular and chronic atrophic gastritis. Erosions, linear antral reddish streaks, subepithelial hemorrhages, and multiple ulcers were diffetrent types of gastric mucosal changes found in reactive gastropathy patients.

Keywords: Gastritis, Gastropathy, Nodular gastritis,, Gastric atrophy, Retrospective analysis

Gastritis and gastropathy are two different mucosal identities found during upper gastrointestinal endoscopies.[1] Gastritis is a microscopic diagnosis, defined by inflammatory infiltrates in histologic examination. Its incidence is 14% in normally looking gastroscopic findings;[2] therefore 5 gastric biopsies are advised to diagnose it.[3] Gastropathy is broadly classified into portal hypertensive,[4] hyperplastic,[5] and reactive.[6] Abnormal gastroscopic findings with normal histology are often due to reactive gastropathy.[6] Acute gastritis[7] can be classified into 2 groups: acute non-erosive gastritis and

acute erosive gastritis. Acute erosive gastritis is identified by gastric mucosal erythema and edema without erosive changes. It is usually caused by helicobacter pylori (Hp). Acute erosive gastritis[8] is also named as reactive gastropathy. In addition to gastric mucosal erythema and edema, erosive changes including reddish streaks, multiple erosions, subepithelial hemorrhages and multiple small ulcers are the endoscopic hallmarks for the diagnosis of reactive gastropathy. Severe infectious gastritis with green black exudate and thick edematous mucosa is known as Phlegmonous gastritis.[9,10] Chronic gastritis[11] is further divided into atrophic gastritis, nodular gastritis, granulomatous gastritis, and many more identities. Thin pale shiny mucosa with prominent subepithelial vasculatures is a diagnostic clue of chronic atrophic gastritis (AG).[12] Chronic nodular gastritis it is diagnosed endoscopically by finding mucosal nodularity with cobblestone appearance.[11] Narrow distal stomach with thick folds, cobble stone appearance and prepyloric ulcers may be due to granulomatous gastritis.[13] Portal hypertensive gastropathy (PHG) and gastric vascular ectasia (GVE)[14] are two types of gastric mucosal changes due to long standing portal hypertension. Endoscopically, PHG is appreciated by mosaic-like pattern; where superimposed red spots discriminate its severe form from its mild form. In GVE, red spots are usually seen without a mosaic background. Hyperplastic gastropathy is characterized by giant gastric folds with epithelial hyperplasia.[15] It can be due to Menetrier's disease or Zollinger Ellison syndrome. The objective of this study was to determine the prevalence of different subtypes of gastritides and gastropathies amongst patients who underwent upper GI endoscopies at Liver clinic, Lahore, Pakistan.

METHODS

This retrospective cohort analysis was conducted at Liver clinic, 250 Shadman Lahore. Amongst the patients who underwent UGIE from 1st July 2011 to 30th June 2014, the patients with endoscopic gastric findings suggestive for different types of gastritis and gastropathy were studied. The mucosal erythema and edema without erosive changes defined acute non-erosive gastritis (ANG), where addition of erosions, ulcers, sub-epithelial hemorrhages and reddish streaks were named as acute erosive gastritis (AEG). Green black exudates in addition to thick edematous folds morphologically defined the Phlegmonous gastritis. Thin pale shiny mucosa with prominent subepithelial vasculatures, and cobblestone appearance due to mucosal nodularity defined the chronic atrophic gastritis and chronic nodular gastritis respectively. In liver cirrhosis patients, mosaic-like pattern of gastric mucosa was named as PH. In patients with portal hypertension, presence of superimposed red spots differentiated severe PHG from its mild form. GVE was also found as red spots, but usually without a mosaic background in these liver cirrhosis patients. The giant gastric folds with epithelial hyperplasia gave us the suspicion of hyperplastic gastropathy. The gender, presence and types of gastritis and gastropathy, and mucosal finding in reactive gastropathy were the qualitative variables, while age and weight of the patients were the quantitative variables. 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.

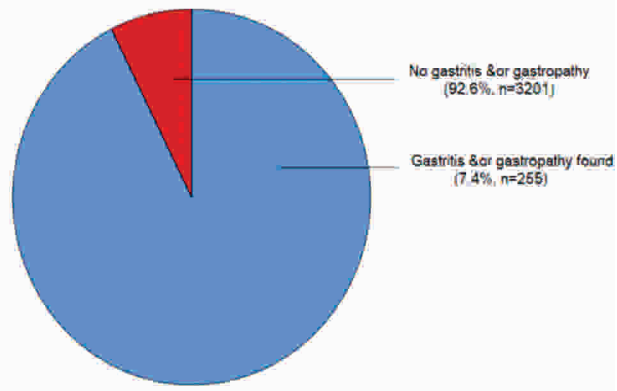
RESULTS

Out of the total of 3456 patients who underwent UGIE, 60.8% were male and 39.2% were female. Their age ranged from 3 to 95 years, with a mean value of 48.54 + 12.96 years. Their mean weight was 71.80 + 16.2 Kilogram, with a range of 13-131 kilogram. 92.6% patients (3201 out of 3456) had endoscopic features suggestive of gastritis and gastropathies. (Picture 1)

Amongst the patients with findings suggestive for gastritis (n=935), 51.8% (n=484) patients had acute non-erosive gastritis, 37.2% (n=349) patients

had reactive gastropathy (acute erosive gastritis), 6.2% (n=58) patients had nodular gastritis and 4.7% (n=44) patients have atrophic gastritis. Amongst patients with findings suggestive for gastropathy (n=2266), majority patients (n=2243, 98.98%) had portal hypertyensive gastropathy (PHG), 0.93% (n=21) patients had prolapse gastropathy and only 0.09% (n=2) patients had hyperplastic gastropathy. (Table 1)

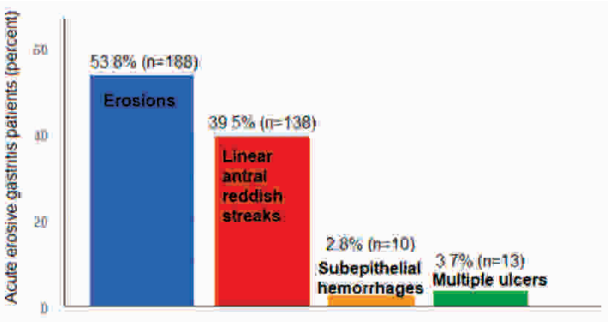
Amongst patients with reactive gastropathy, dominant gastric findings suggestive of the diagnosis were erosions (53.8%, n=188), linear antral reddish streaks (39.5%, n=138), subepithelial hemorrhages (2.8%, n=10) and multiple gastric ulcers (3.7%, n=13). (Picture 2)



Picture 1: *Prevalence of Gastritis and Gastropathy as Gastric Findings amongst Patients who Underwent Upper GI endoscopy (n=3201/3456)*

Table 1: *Frequency-Percentage Distribution of Endoscopic Classes of Gastritis and Gastropathy among upper GI Endoscopies (n = 3201/3456)*

Gastritis/ gastropathy	Frequency (Percent)
Gastritis (30.8%, n=1070)	
1. Acute non-erosive gastritis	555 (51.9%)
2. Reactive gastropathy	401 (37.5%)
3. Nodular gastritis	68 (6.4%)
4. Atrophic gastritis	46 (4.3%)
Gastropathy (69.2%, n=2404)	
5. Portal Hypertensive gastropathy	2375 (98.8%)
6. Prolapse gastropathy	25 (1.0%)
7. Hyperplastic gastropathy	4 (0.17%)



Picture 2: *Dominant Findings in Acute Erosive Gastritis Patients.*

DISCUSSION

On the basis of endoscopic and histologic features, classification and subclassification of gastritides and gastropathies narrow our differentials because etiopathogenesis of most of these subclasses is known. Acute erosive gastritis is generally caused by helicobacter pylori (Hp) infection.[16] In addition to Hp, other infective organisms of stomach include CMV, measles, mycobacterium, syphilis and fungi. Phlegmonous gastritis[9,10] is seen in alcoholism, leukemia, AIDS, or corrosive intake patients. In acute erosive gastritis/reactive gastropathy, mucosa is damaged by medicine, toxins, bile reflux, stress, radiations, and ischemia.[17] Microscopically, granulomas are seen in granulomatous gastritis.[13] Sarcoid, TB and CD should be considered as the differential diagnoses. Hp gastritis is the common etiology for chronic nodular gastritis; however other causes are CD, syphilitic gastritis, lymphocytic gastritis and collagenous gastritis. In chronic atrophic gastritis (AG), the findings are distributed in corpus and corpus as well as antrum of stomach in its subtypes (Autoimmune AG, Environmental AG) respectively. The later is most commonly due to Hp gastritis. Portal hypertensive gastropathy is the sequela of portal hypertension, which may be due to pre-hepatic, hepatic and post-hepatic causes of rise in portal pressure. Prolapse gastropathy is an identitiy usually seen in hiatal hernia patients.[18] Hyperplastic gastropathy can be due to Menetrier's disease or Zollinger Ellison syndrome.[19]

The national and even internataional data regarding the frequency of different types of gastritides and gastropathies is scarce. Our study provided first time the whole amplification about the prevalances of different types of gastritides and gastropathies in our population. Our study also explained the percentage distribution of different types of endoscopic findings in reactive gastropathy patients like erosions, linear antral reddish streaks, subepi-

thelial hemorrhages, and multiple ulcers. Medicines and toxins are the commonest etiology for reactive gastropathy. Bile reflux gastropathy is common after surgery of stomach or gallbladder and even after sphincterotomy. Further larger studies are required to validate the association between etiology of reactive gastropathy and type of mucosal erosive changes. In our study, 29.2% patients had gastritides and 70.8% had gastropathies. In a similar study from Uganda,[20] gastritides were 40.2% diagnoses in patients who underwent UGIE. In 2010, Abbasi et al[4] found the frequency of PHG in liver cirrhosis of 79.27%, while in our study, among all diagnosed gastropathies, 98.98% were portal hypertension related gatropathy. All the data suggests that hepatic cirrhosis is the main burden in the medical and gastroenterology departments in Pakistan, where PHG is the commonest gastric finding during all upper gastrointestinal endoscopies performed in our GI suites followed by different types of gastritides, especially Hp gastritis.

CONCLUSION

Portal hypertensive gastropathy was the commonest gastric finding in upper gastrointestinal endoscopies amongst our patients. This reflects the high burden of liver cirrhosis in our country. Other gastropathies like prolapse and hyperplastic were seen in a very little proportion of the patients. Acute non-erosive gastritis was the commonest type of gastritis followed by acute erosive, chronic nodular and chronic atrophic gastritis. Erosions, linear antral reddish streaks, subepithelial hemorrhages, and multiple ulcers were diffetrent types of gastric mucosal changes found in reactive gastropathy patients.

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CARDIAC WALLS INVOLVED IN ACUTE ST ELEVATION MYOCARDIAL INFARCTION (STEMI) PATIENTS AND ASSOCIATED FACTORS

Muhammad Shahid[a], Muhammad Irfan[a], Qamar Rafiq[a], Muhammad Rashid Ali [c], Rao Hashim Idrees[a], Shahzad Majeed Bhatti[b]

[a]Gujranwala Medical College/Teaching Hospital, Gujranwala, Pakistan

[b]Allama Iqbal Medical College / Jinnah hospital, Lahore, Pakistan

Abstract

Objectives: To determine different cardiac walls involved in acute ST elevation myocardial infarction (STEMI) patients and their associations with various factors at tertiary care hospital, Gujranwala, Pakistan.

Methods: In this cross-sectional study, patients admitted with STEMI, of both genders, and all age groups, who were treated with Streptokinase injection were included. Independent sample T test and Chi-square test for independence were used for quantitative and qualitative variables respectively to determine the significant factors associated with inferior wall STEMI. Then, binary logistic regression analysis was also performed on the significant factors. The p values were taken statistically significant if < 0.05

Results: Amongst 668 STEMI patients, 43.7% had inferior wall involved, who had significantly higher BMI (p<0.001), higher door to needle time (p<0.001), lower pulse rate at presentation (p<0.001), lower systolic and diastolic BP at presentation (p<0.001, p<0.001), lower maximum ST segment elevation on ECG (P<0.001), higher serum creatinine (p=0.040), and lower at 1st post-admission day pulse rate (p<0.001), systolic BP (p=0.008), and diastolic BP (p=0.001), higher in-hospital mortality rate (p=0.014) and more right ventricle involvement (p<0.001). The binary logistic regression model was statistically significant, p<0.05, and explained 28.1% (Nagelkerke R2) of the variance and correctly classified 96.3% of cases.

Conclusion: The STEMI patients had a vast variety in term of cardiac wall involvement where inferior wall involvement was the commonest one. Patients with inferior wall STEMI had relatively higher BMI, door to needle time, serum creatinine, right ventricular involvement as well as in-hospital mortality. Those patients also had lower pulse rate and blood pressure level at presentation as well as on 1st post admission day. Majority factors were modifiable, so in-hospital mortality associated with inferior wall STEMI could be reduced by special attention on them.

Keywords: STEMI, in-hospital mortality rate, cross-sectional study, SPSS

Acute ST-elevation myocardial infarction (STEMI) is a lethal event in which transmural myocardial necrosis occurs due to complete occlusion of one or more of the coronary arteries.[1] In USA, the incidence of first MI in both genders is approximately stable during last 10 years, that is 1.1% and 1.7% per year in men and women, respectively.[2] Our people are more prone to MI. Its annual incidenc in subcontinent is approx 6.44%.[3] Among acute coronary syndrome patients, approximately 38% have STEMI.[4] The most effective treatment for STEMI is the immediate restoring the patency of the occluded artery either by PCI or fibrinolysis.[5] The American Heart Association guidelines suggest primary percutaneous coronary intervention (PCI) as the preferred treatment for STEMI patients,[6] however in our settings fibrinolysis is used widely due less availability of PCI. The ECG pattern enable us to localize the myocardial injury place.[7] Changes in ECG leads V1-V2 correspond to septal wall involement, leads V3-V4 to the anterior wall, leads I and aVL to the lateral wall, leads II, III and aVF to the inferior wall, and mirror pattern (high R wave) in leads V1-V3 correspond to the basal part of infero-posterior wall involvement.[8] The knowledge of cardiac wall involved is very important for the

prediction of potential complications and subsequent therapeutic strategy.[9] For example, anterior MI carries worst prognosis of all infarct locations, mostly due to large infarct size.[10] Acute inferior MI is sometimes complicated by hypotension or bradycardia.[11] Similarly, administring nitroglycerin (to relieve ischemic chest pain) may cause hemodynamic collapse in right ventricular infarction patient. Therefore, the objective of the present study was to determine the frequency distribution of acute ST elevation myocardial infarction (STEMI) according to cardiac wall involved on ECG. The study will also find the significant factors associated with inferior wall STEMI at tertiary care hospital, Gujranwala, Pakistan.

METHODS

The data for this cross-sectional study was collected by purposive sampling, from the Department of Cardiology, GMC Teaching hospital, Gujranwala from June 2017 to May 2018. The patients admitted with STEMI, of both genders, and all age groups, who were treated with Streptokinase injection were included. Cardiac wall involved by STEMI was noted on ECG, and patients were categorized into two groups; one with inferior wall involved and second with other than inferior wall involved. Statistical Package for Social Science (SPSS), version 25 was used to perform the statistical analysis. Age, BMI, time from onset of symptoms till arrival at hospital in minutes, door to needle time in minutes, baseline pulse, systolic BP at presentation, diastolic BP at presentation, minimum ST segment elevation, maximum ST segment elevation, serum creatinine conc., serum sodium conc., serum potassium conc., pulse rate, systolic BP, diastolic BP at 1st post-admission day were the quantitative variable, while gender, history of smoking, hypertension, diabetes mellitus, personal H/O IHD, History of IHD in male family member of age <55years, History of IHD in female family member of age <45years obesity, cardiac wall involved by STEMI, right ventricular involvement, ST segment settlement >50% at 1st post-admission day, and outcome of hospitalization were the qualitative variables. Independent sample T test and Chi-square test for independence were used for quantitative and qualitative variables respectively to determine the significant factors / predictors associated with inferior wall involved by STEMI. Then, binary logistic regression analysis was also performed on the significant factors associated with inferior wall involvement. The p values were taken statistically significant if < 0.05

RESULTS

Amongst 668 patients who presented with STEMI, 43.7% had inferior wall involvement while 56.3% had other than inferior wall involvement. The detailed frequency distribution of cardiac wall involvement by STEMI was as follow: 9.1% (n=61) involved anterior wall, 17.8% (n=119) antero-septal wall, 11.8% (n=79) antero-lateral wall, 9.7% (n=65) extensive anterior wall, 12.1% (n=8) antero-inferior wall, 3% (n=20) lateral wall, 1.8% (n=12) posterior wall, 1.8% (n=12) postero-lateral wall, 29.9% (n=200) inferior wall, 5.4% (n=36) inferior wall plus right ventricle, 3% (n=20) infero-lateral wall, 1.8% (n=12) infero-lateral wall plus right ventricle, 3% (n=20) infero-posterior wall, 0.6% (n=4) infero-posterior wall plus right ventricle. (Picture 1 & 2). As compared to patients with STEMI involving other than inferior wall, inferior wall STEMI patients had statistically significantly higher BMI ($p<0.001$), higher door to needle time ($p<0.001$), lower pulse rate at presentation ($p<0.001$), lower systolic and diastolic BP at presentation ($p<0.001$, $p<0.001$), lower maximum ST segment elevation on ECG ($P<0.001$), higher serum creatinine ($p=0.040$), and lower at 1st post-admission day pulse rate ($p<0.001$), systolic BP ($p=0.008$), and diastolic BP ($p=0.001$) (Table 1). As compared to other walls involving STEMI, inferior wall STEMI was significantly associated with right ventricle involvement ($p<0.001$) and relatively higher in-hospital mortality rate ($p=0.014$) (Table 2) A binary logistic regression

Table 1: *Associations between Various Quantitative Variables and Inferior Wall Involved among STEMI Suffering Patients Treated with Streptokinase (n = 668) **

Quantitative variables	Cardiac wall involved by STEMI		Mean difference	p-value
	Inferior wall (mean + SD)	Other than inferior wall (mean + SD)		
1. Age (years)	54.42 ± 11.97	53.34 ± 12.66	1.077	.264
2. BMI (Kg/m^2)	27.77 ± 4.18	26.51 ± 4.06	1.2642	.000
3. Time till arrival (minutes)[1]	256.65 ± 312.49	295.43 ± 385.79	-38.778	.163
4. Door to needle time (minutes)	34.26 ± 45.32	22.64 ± 25.07	11.619	.000
5. Baseline pulse (per minute)	80.67 ± 19.83	90.10 ± 17.32	-9.429	.000
6. Baseline systolic BP (mmHg)	126.30 ± 28.70	135.14 ± 23.54	-8.846	.000
7. Baseline diastolic BP (mmHg)	79.54 ± 20.61	84.89 ± 15.10	-5.353	.000
8. ST segment elevation, minimum (mm)	2.449 ± 1.46	2.553 ± 1.57	-.1046	.379
9. ST segment elevation, maximum (mm)	4.332 ± 3.09	5.356 ± 3.21	-1.0242	.000
10. Serum creatinine (mg/dl)	1.191 ± 1.14	1.061 ± 0.40	.1305	.040
11. Serum Sodium (mEq/L)	137.46 ± 4.18	136.74 ± 6.13	.718	.087
12. Serum Potassium (mEq/L)	3.83 ± 0.64	3.76 ± 0.66	.0757	.136
13. Pulse at 1st post admission day	78.54 ± 12.70	87.26 ± 15.30	-8.711	.000
14. Systolic PB at 1st post admission day	111.64 ± 18.54	115.43 ± 17.93	-3.782	.008
15. Diastolic PB at 1st post admission day	72.19 ± 13.19	75.53 ± 13.11	-3.340	.001

*Independent sample T-test was used; 1=Time from onset of symptoms till arrival at hospital (minutes)

Table 1: *Qualitative Factors Associated with Outcome of Hospitalization among STEMI Suffering Patients Treated with Streptokinase (n = 668) **

Predictors / Factors	Cardiac wall involved by STEMI		Total	p-value
	Inferior wall	Other than inferior wall		
Gender:				
Male	223 (76.4%)	292 (77.7%)	515 (77.1%)	0.711
Female	69 (23.6%)	84 (22.3%)	153 (22.9%)	
History of smoking:				
Yes	162 (55.5%)	200 (53.2%)	362 (54.2%)	0.584
No	130 (44.5%)	176 (46.8%)	306 (45.8%)	
History of diabetes mellitus:				
Yes	81 (27.7%)	116 (30.9%)	197 (29.5%)	0.394
No	211 (72.3%)	260 (69.1%)	471 (70.5%)	
History of hypertension:				
Yes	159 (54.5%)	202 (53.7%)	361 (54%)	0.876
No	133 (45.5%)	174 (46.3%)	307 (46%)	
Personal history of IHD:				
Yes	85 (29.1%)	108 (28.7%)	193 (28.9%)	0.932
No	207 (70.9%)	268 (71.3%)	475 (71.1%)	
History of IHD in male family member of age <55years				
Yes	33 (11.3%)	48 (12.8%)	81 (12.1%)	0.633
No	259 (88.7%)	328 (87.2%)	587 (87.9%)	
History of IHD in female family member of age <45years:				
Yes	29 (9.9%)	52 (13.8%)	81 (12.1%)	0.151
No	263 (90.1%)	324 (86.2%)	587 (87.9%)	
Obesity:				
Yes	77 (26.4%)	76 (20.2%)	153 (22.9%)	0.064
No	215 (73.6%)	300 (79.8%)	515 (77.1%)	
Right ventricular involvement:				
Yes	53 (18.2%)	0 (0%)	53 (7.9%)	<0.001
No	239 (81.8%)	376 (100%)	615 (92.1%)	
ST elevation settled >50% at 1st post-admission day:				
Yes	239 (81.8%)	288 (76.6%)	527 (78.9%)	0.105
No	53 (18.2%)	88 (23.4%)	141 (21.1%)	
Outcome of hospitalization:				
Death	17 (5.8%)	8 (2.1%)	25 (3.7%)	0.014
No death	275 (94.2%)	368 (97.9%)	643 (96.3%)	

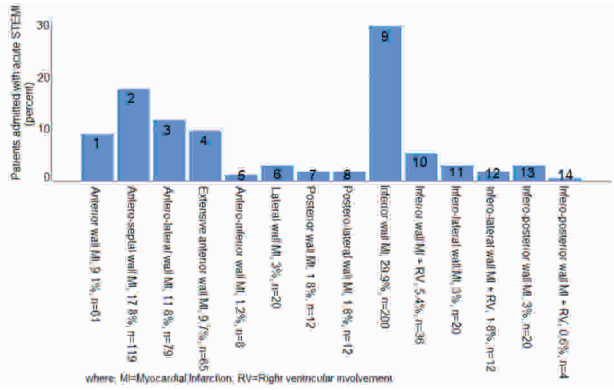
*Chi-square test for independence was used

Table 3: *Binary Logistic Regression Analysis to Predict Inferior Wall Involvement by STEMI Suffering Patients Treated with Streptokinase (n = 668) **

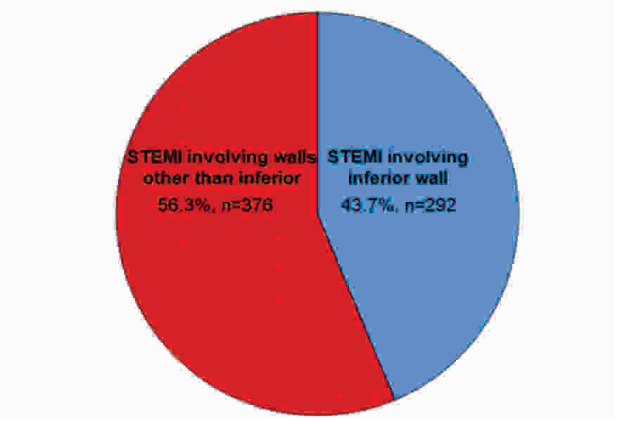
Risk Factors	B	S.E.	Wald-Statistic	p-value	Odds Ratio	95% C.I. for EXP(B)	
						Lower	Upper
1. **BMI** (Kg/m^2)	-.088	.023	14.873	.000	.915	.875	.957
2. **Door to needle time** (minutes)	-.012	.003	16.250	.000	.988	.982	.994
3. **Baseline pulse** (per minute)	.023	.006	15.264	.000	1.023	1.011	1.035
4. **Baseline systolic BP** (mmHg)	.008	.007	1.365	.243	1.008	.995	1.022
5. **Baseline diastolic BP** (mmHg)	.005	.010	.238	.626	1.005	.986	1.024
6. **ST segment elevation, maximum** (mm)	.141	.035	16.060	.000	1.151	1.075	1.233
7. **Serum creatinine** (mg/dl)	-.274	.119	5.319	.021	.760	.602	.960
8. **Pulse at 1st post admission day**	.044	.008	29.249	.000	1.044	1.028	1.061
9. **Systolic PB at 1st post admission day**	-.006	.012	.306	.580	.994	.971	1.016
10. **Diastolic PB at 1st post admission day**	.011	.015	.531	.466	1.011	.982	1.041
11. **Outcome of hospitalization** Death/ No death)	-.432	.520	.692	.405	.649	.234	1.797
Constant	-4.437	1.109	15.995	.000	.012		

Cox & Snell R Square = 21.0%, Nagelkerke R Square = 28.1%

analysis was performed to ascertain the likelihood association of various factors/ variables with inferior wall involvement. The logistic regression model was statistically significant, p<0.05. The model explained 28.1% (Nagelkerke R2) of the variance in the group of STEMI patients with inferior wall involved and correctly classified 96.3% of cases. Increasing BMI was associated with an increased likelihood of involving inferior wall by STEMI. Similarly, higher door to needle time, lower serum creatinine, comparatively less ST segment elevation (maximum), lower pulse rate at presentation and at 1st post-admission day were associated with an increased likelihood of involvement of inferior wall by STEMI (Table 3).



Picture 1: *Frequency Distribution of different Classes of Acute ST Segment Myocardial Infarction (STEMI) According to Cardiac Walls Involvement*



(n=668)

Picture 2: *Distribution of Acute ST Elevation Myocardial Infarction (STEMI) Considering Inferior Wall Involvement (n=668)*

DISCUSSION

In majority studies, myocardial infarction found commonestly involving anterior and inferior walls. In a study of STEMI from India, 72% patients presented with anterior wall MI, 21.5% with inferior wall MI, 4% with posterior wall MI, and 2.5% with right ventricular MI.[12] In another study, anterior STEMI was reported in 42% patients, inferior STEMI in 42%, inferior STEMI with right ventricular involvement in 11% of all patients, and lateral STEMI in 5% patients.[13] M Javed Iqbal et al found the anterior wall MI as the commonest one (53.8%) followed by inferior wall MI (30.4%) and lateral

wall MI (7.9%).[14] In a similar study from Faisalabad, 43% patients presented with inferior wall STEMI, 43% with antero-septal STEMI, and rest with other walls involvement.[15] Similarly, in our study, 43.7% STEMI patients had inferior wall involved and rest 56.3% had other than inferior wall involvement. In our data, it was laso seen that patients suffering inferior wall STEMI had higher BMI, while patients with other than inferior walls involved had lower BMI. The significance of these findings needs further studies with large sample size. In literature, multiple studies revealed the worst prognosis and higher incidences of in-hospital mortality with anterior wall MI as compared to inferior wall MI.[10,16] Peter H. Stone et al compared anterior wall MI with inferior wall MI. He found that patients with anterior MI had higher incidences of in-hospital mortality (11.9 vs 2.8%), and heart failure (41 vs 15%) compared to patients with inferior MI.[17] In our study, in hospital mortality was higher with inferior wall MI compared to other walls MIs (5.8% vs 2.1%, p=0.014). There were multiple reasons for higher in-hospaital mortality with inferior wall MI in our patients.

Firstly, higher door to needle time is associated with higher mortality.[18] Ideally, for patients in whom fibrinolysis is indicated, the hospital door-to-needle time should be within 30 minutes for patients.[(19)] In our patients, door to needle time was significantly higher in inferior wall MI patients compared to patients with other than inferior walls involved (mean value 34.26 vs 22.64 sec, p<0.001). Secondly, a significant number of inferior wall MI patients (18.2%, p<0.001) had right ventricular involvement in the studied population. It is well known that right ventricular involvement imposes a higher risk of adverse events.[20] Thirdly, Hypotension, bradycardia and pre-renal azotemia, all add negative burden in MI patients,[21] where in our studied group, patients with inferior wall STEMI had lower pulse rate and blood pressure level at presentation as well as on 1st post admission day and relatively higher serum creatinine value. Hence, finding of right ventricular involvment, hypotension, higher door to needle time and azotemia resulted higher in-hospital mortality in our inferior wall STEMI patients. By addressing the modifiable factors, in-hospital mortality associated with inferior wall STEMI could be reduced in our patients.

CONCLUSION

The STEMI patients had a vast variety in term of cardiac wall involvement where inferior wall involvement was the commonest one. Patients with inferior wall STEMI had relatively higher BMI, door to needle time, serum creatinine, right ventricular involvement as well as in-hospital mortality. Those patients also had lower pulse rate and blood pressure level at presentation as well as 1st post admission day. All these findings are associated with each other. Increased door to needle time with lower vital signs, right ventricle and renal involvement, perhaps due to hypovolemia-associated ATN, all are responsible for higher in-hospital mortality in inferior wall patients. Majority factors were modifiable, so in-hospital mortality associated with inferior wall STEMI could be reduced by special attention on them.

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COMPARISON OF BOTH GENDERS FOR MEAN ALVEOLAR BONE SCORE AMONG OBESE AND NON-OBESE PATIENTS.

Sobia Malik[1], Mohammad Sohail[2], Asif Hanif [3], Ayyaz Ali Khan[4], Arshad Kamal Butt[4], Iqra Waheed[5]

[1]Oral Anatomy Federal Postgraduate Institute / Shaikh Zayed Hospital, Lahore; [2]Professor, Department of Anatomy, FPGMI/ Shaikh Zayed Hospital, Lahore; [3]Head of Biostatistics Department, GDPGMI, Lahore[4]Associate Professor, Department of Anatomy, FPGMI/ Shaikh Zayed Hospital. Lahore; [5]Biostatistics, CSAS, PU, Lahore

Abstract

Background: Obesity is one of the most significant health risks of modern society, and is now recognized as a major health concern in both developed and developing countries. The prevalence of obesity is increasing at alarming rates, approaching epidemic proportions, particularly among children and young adults. Recently, an association between obesity and periodontal disease has been suggested. Evidence is rapidly mounting indicating obesity as an independent or aggravating risk factor for several diseases including alveolar bone loss.

Aims and Objectives: The aim of this study was to compare the mean alveolar bone score between obese and non-obese patients of both genders with periodontal disease.

Material and methods: 100 patients of established periodontal disease where were selected which was diagnosed by applying CPITN criteria. The age range of patients was 30-40 years. They were divided into two groups i.e. obese and non-obese groups. There were 50 subjects in each group. The criterion for diagnosis obesity was based on body mass index (BMI). The selection of all 100 subjects was done according to exclusion and inclusion criteria which possibly excluded all other factors which might enhance alveolar bone loss except obesity. Patients were divided into two groups according to their weight; obese and non- obese. Then panoramic radiographs of all subjects were taken and alveolar bone loss was measured. Then to rule out the effect of age on alveolar bone loss an age-related alveolar bone score was calculated for all subjects of both; obese and non-obese group. Two groups were stratified in male and female gender to control the effect of this confounding variable.

Results: The comparison of AB score between obese versus non-obese cases showed that there were This difference showed that decreased AB score indicating alveolar bone loss is more in obese as compared to non-obese patients and is statistically significant.

Conclusion: As there were more patients in obese group which had lower alveolar bone score. So in middle aged patients of periodontal disease belonging to urban Pakistani population obesity as assessed by body mass index (BMI) is associated with increased alveolar bone loss. Whether male or females patient, if they are obese then both are at risk of alveolar bone loss.

Key words: Alveolar bone, BMI, AB Score

Obesity is one of the most significant health risks of modern society, and is now recognized as a major health concern in both developed and developing countries.[1] The prevalence of obesity is increasing at alarming rates, approaching epidemic proportions, particularly among children and young adults.[2]

Recently, an association between obesity and periodontal disease has been suggested.[3] Furthermore, the results of the Third National Health and

Correspondence: Dr. Sobia Malik, Department of Dentistry, Federal Postgraduate Institute / Shaikh Zayed Hospital, Lahore, Email: drsobia11malik@gmail.com

Nutrition Examination Survey conducted in the United States of America showed that waist to hip ratio, body mass index (BMI), fat free mass and log sum subcutaneous fat were significantly correlated to periodontitis, signifying that abnormal fat metabolism may be an important factor in the pathogenesis of periodontal diseases.[4] Evidence is rapidly mounting indicating obesity as an independent or aggravating risk factor for several diseases, including coronary heart disease, osteoarthritis and type 2 diabetes mellitus.[5]Studying the relationship between obesity and periodontal disease is, therefore, important since this association could further contribute to increased morbidity of these diseases in overweight or obese individuals.[6] This study targeted the young adults (age range 30-40 years) because the influence of obesity on periodontal disease in older participants might be confounded by the age factor—many older individuals gain some weight as a part of the aging process. The aim of this study is to compare the mean alveolar bone score of both genders in obese and non-obese patients. So that it may come to know that in which group there are more chances of alveolar bone loss.

METHODS

This case control study was conducted department of Anatomy Federal Postgraduate Medical Institute Lahore in collaboration with department of Dentistry and department of Radiology Shaikh Zayed Hospital, Lahore. 100 patients were included from OPD of Dentistry department who had age between 30-40 years and diagnosed to have periodontal disease on Community Periodontal Index of Treatment Needs (CPITN) and were divided into two groups of obese (cases) and non-obese (controls). Criteria for diagnosis of obesity was BMI>30kg/m^2 and non-obese was BMI<25kg/m^2. Patients having diabetes, smokers, alcohol users, having H/O/ fracture because of Osteoporosis or malignancy, having Vitamin D deficiency or autoimmune diseases were excluded or who did not give informed consent. Radiographs were also evaluated to assess the degree of alveolar bone loss in both groups.

Statistical Analysis:

Data was entered and analyzed through SPSS version 11. Mean+SD was calculated for quantitative variables like age and alveolar bone score. Frequency and percentage was calculated for qualitative variables like gender, and number of obese and non-obese patients in different alveolar bone score groups. Data was firstly stratified for gender and then for obese and non-obese groups to access the significance of alveolar bone scores.

RESULTS

In this study there were 43 males and 57 females were involved with the mean age range of 35.10+2.241 years (age range 30-40 years). Mean age of male and female patients were 34.74±2.071 years and 35.37±2.342 years respectively. The mean alveolar bone score for over all patients was 64.51+8.212 (see table 1). The mean Alveolar bone score in male group was 64.09±9.707 while mean Alveolar bone score in female group was 64.82± 6.952. Among males the mean Alveolar bone score in obese group was 56.4±3.883 while mean Alveolar bone score in non-obese group was 72.90±6.181 (p-value 0.000**, 95% Cl; 13.233, 19.767) and among females the mean Alveolar bone score in obese group was 59.44±4.569 while mean Alveolar bone score in non-obese group was 69.67±4.838. This difference was statistically significant (p-value 0.000**, 95% Cl; 7.732, 12.728) (see table 3). When comparing male and female gender for obese group, the difference was statistically significant (p-value 0.014*. 95% Cl; 0.637. 5.443) and comparing male and female gender for non-obese group, the difference was not statistically significant (p-value 0.057NS, 95% Cl; -0.103, 6.563) (see table 3).

Table 1: Characteristics of Patients Included in the Study

Mean Age of all patients	35.10+2.241 years
Males	34.74+2.071 years
Females	35.37+2.342 years
Gender:	
Male	43
Female	57
AB score of all patients	64.51+8.212
Male	64.09+9.707
Female	64.82+6.952
p-value	0.661 NS

Table 2: Gender Distribution in Obese vs. Non Obese Group

Group	Gender of patient		Total
	Male	Female	
Obese	23	27	50
Non-obese	20	30	50
Total	43	57	100

Table 3: Stratification of Data for Gender Distribution

AB score	Male	Female	p-value
Mean AB score for Obese	56.4±3.883	59.44+4.569	0.014*
Mean AB score for Non-obese	72.90+6.181	69.67±4.838	0.057NS
p-value	0.000**	0.000**	

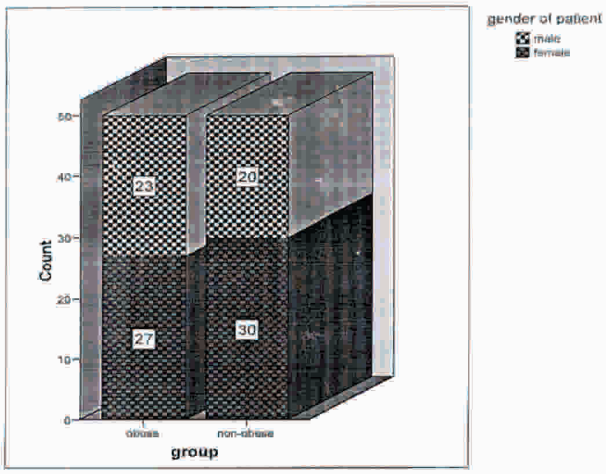

Figure 1: *Gender Distribution of Obese and Non-Obese Patients*

Table 4: Stratification of Obese and non- Obese patients for gender difference

AB score	Obese	Non-obese
Mean AB score for Male	56.4±3.883	72.90±6.181
Mean AB score for Female	59.44±4.569	69.67±4.838
p-value	0.016**	0.044**

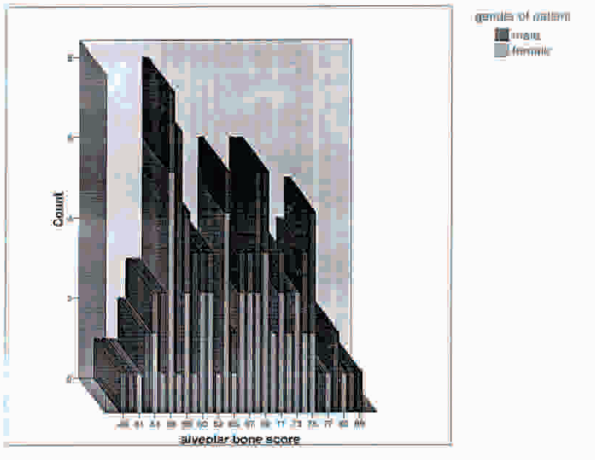

Figure 2: *Comparison of Alveolar Bone Score of both Genders in Obese vs. Non Obese Group*

DISCUSSION

The present findings showed a statistically significant positive relationship between obesity and periodontal measurements of CPI in male and female participants. In this study there were 43 males and 57 females were involved with the mean age range of 35.10+2.241 years (age range 30-40 years). Mean age of male and female patients were 34.74± 2.071 years and 35.37±2.342 years respectively.

Obesity has been postulated to reduce blood flow to the periodontal tissues, promoting the development of periodontal disease.[7] Furthermore, obesity may enhance immunological or inflammatory disorders, which might be the reason obese subjects tend to exhibit escalating poor periodontal status relative to non-obese individuals.[8] The mean alveolar bone score for over all patients was 64.51+ 8.212. The mean Alveolar bone score in male group was 64.09+9.707 while mean Alveolar bone score in female group was 64.82+6.952. Among males the mean Alveolar bone score in obese group was 56.4+3.883 while mean Alveolar bone score in non-obese group was 72.90+6.181 (p- value 0.000**, 95% Cl; 13.233, 19.767) and among females the mean Alveolar bone score in obese group was 59.44+4.569 while mean Alveolar bone score in non-obese group was 69.67+4.838. This difference

was statistically significant (p-value 0.000**, 95% Cl; 7.732, 12.728). When comparing male and female gender for obese group, the difference was statistically significant (p-value 0.014*, 95% Cl; 0.637. 5.443) and comparing male and female gender for non-obese group, the difference w:as not statistically significant (p-value 0.057NS, 95% Cl; -0.103, 6.563). Numerous studies have confirmed a reduction in alveolar bone crest height with age both in healthy subjects and in those with periodontal disease.[9-13] However, wide variations are found in the degree of proximal alveolar crest loss within the same mouth, between individuals and among different types of periodontitis.[9,14-16] Studies normally use clinical probing and radiographic measurements to determine the rate of periodontal attachment and radiographic bone loss. According to our study obese males are at more risk of losing alveolar bone as compared to females but in non-obese group, females were at more risk of alveolar bone loss. But according to literature, there is a significant relationship between obesity and alveolar bone loss and according to same study females are at more risk of alveolar bone loss but our results opposing the literature.[17] No more studies are available to confirm the results except one study done by Alabdulkarim et al.[17] Further studies are required to clarify the ambiguity in the results with larger sample size.

CONCLUSION

As there were more patients in obese group which had lower alveolar bone score. So in middle aged patients of periodontal disease belonging to urban Pakistani population obesity as assessed by body mass index (BMI) is associated with increased alveolar bone loss. Whether male or females patient, if they are obese then both are at risk of alveolar bone loss.

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CLINICO-ETIOLOGICAL SPECTRUM OF STEVENS JOHNSON SYNDROME (SJS) & TOXIC EPIDERMAL NECROLYSIS (TEN) AMONG PATIENTS OF CUTANEOUS ADVERSE DRUG REACTIONS (CADRS) IN A TERTIARY CARE UNIT

Shaista Umbreen, Lamees Mahmood Malik, Sahrish Rashid, Naima Aliya, Khadija Malik, Muhammad Nasir, Tariq Rashid.

Department of Dermatology, Unit 1. Allama Iqbal Medical College / Jinnah Hospital Lahore.

Abstract

Objective: To study the clinico-etiological spectrum of SJS & TEN among patients of CADRs in a tertiary care hospital in Lahore.

Methods: A total of 210 patients presenting with adverse drug reactions were studied. The assessment for ADR was done by using Naranjo Algorithm scale and all patients were examined for various clinical patterns.Patients of SJS and TEN were diagnosed on clinical examination. Relevant details regarding drug intake including duration and type of drug, dose taken etc were obtained and all information was recorded on pre designed proforma.

Results: SJS was observed in 20/210 (20 %) and TEN was observed in 10/210 (4.8 %) of the patients presenting with CADRs. Antibiotics were implicated in most of the cases of both SJS (40 %) and TEN (50 %), followed by miscellaneous drugs (30 & 40 % respectively in SJS and TEN patients).

Conclusion: Stevens Johnson syndrome and Toxic Epidermal Necrolysis together accounted for 14.3% of the CADRs observed, with most of these being caused by antibiotics.

Key Words: Cutaneous Adverse Drug Reactions (CADRs), Stevens Johnson Syndrome (SJS), Toxic Epidermal Necrolysis (TEN)

An adverse drug reaction (ADR) has been defined as any noxious, unintended effect of a drug which occurs at a dose used in humans for prophylaxis, diagnosis, therapy or modification of physiological functions.[1] A cutaneous adverse drug reaction (CADR) is any undesirable change in the structure or function of the skin, its appendages or mucous membranes and it encompasses all adverse events related to drug eruption, regardless of the etiology.[2]

Adverse drug reactions are responsible for significant morbidity and mortality, being responsible for 5-8 % of hospital admissions and 5th leading cause of death worldwide. Besides CADRs are the commonest ADRs (45 %), being responsible for 2 % of hospital admissions.[3]

Most cutaneous drug reactions are non-serious but some are severe and potentially life-threatening include angioedema, erythroderma, Stevens Johnson Syndrome (SJS) and toxic epidermal necrolysis (TEN), which constitute 2.6% to 7% of all drug reactions.[4]

SJS comprises extensive erythema multiforme of the trunk and mucous membranes, accompanied by fever > 100°C, malaise, myalgia, and arthralgia. TEN (Lyell's syndrome) is characterized by extensive sheet-like skin erosion with widespread purpuric macules or flat atypical target lesions, accompanied by severe involvement of conjunctival, corneal, irideal, buccal, labial and genital mucous membranes. TEN is usually acute and epidermal necrosis involves > 30% of body surface area. It can be distinguished from SJS, in which by definition, the total surface of body surface area detachment is <10 %.[5]

Numerous new drugs are being introduced,

with each having the potential of producing CADRs. Skin reactions can be induced by almost any drug with some groups being more notorious, like antibiotics, non-steroidal anti-inflammatory drugs (NSAIDs) and anti-epileptics, having drug eruption rates around 1– 5 %.[1]

Current study was done to determine the frequency of serious CADRs, TEN and SJS.Skin changes due to other etiologies are sometimes incorrectly attributed to drugs. The pattern of cutaneous reactions differs among various drugs, and hence knowledge of drugs that can cause CADRs may help physicians in choosing safer drugs.

METHODS

This was across sectional study conducted at Dermatology department unit I, Jinnah Hospital, Lahore for a period of six months from Nov 2015 to May 2016. A total of 210 Patients of both genders, age 20-65 years with a diagnosis of ADRs using Naranjo Algorithm scale[7] and having a score > 5 were enrolled in the study. Patients with severe uncontrolled diabetes mellitus, thyroid disease, pregnancy and lactating females and those with comorbid dermatological conditions were excluded. After written informed consent, detailed history including the presenting complaints, duration of illness, type of drug, duration of the drug intake, past history of the drug allergy was recorded. Patients of SJS and TEN were diagnosed clinically by thorough cutaneous examination. The identification of causative drug was done by history and by reviewing the patients medical records and the prescriptions. A positive temporal relationship with the drug and CADR was established. All information was recorded on a predesigned proforma. At the end of the study the data was analyzed by SPSS version 20.

RESULTS

A total of 210 patients with cutaneous adverse drug reactions (CADRs) were enrolled in this study. Out of these 30 patients (14.3%) suffered from serious CADRs (SJS and TEN). Of these, 20 patients (9.5 %) had SJS and 10 (4.8 %) had TEN. Minimum and maximum age of the patients was 20 and 35 years respectively, with a mean of 27.6 ± 5.29 years. Fifty five percent of the patients with SJS were older than 25 years while 45 % were younger. Similarly, 80% of patients with TEN were older while 20% were younger then 25 years of age. (Table 1) There was a greater number of females (60%) in SJS patients while in patients with TEN males outnumbered females (60%). (Table 1)Regarding the causative agents in majority of the cases of SJS (40%) culprit drugs were antibiotics (quinolones, sulphonamides and penicillin). This was followed by miscellaneous drugs (30%) and NSAIDs (20%). In the TEN patients majority (50%) were caused by antibiotics, followed by miscellaneous drugs (40%) (Table 2)

Table 1: *Age and Gender Distribution of Patients of SJS & TEN*

Drug Reaction	Age		Gender	
	≤ 25 years	> 25 years	Male	Female
Stevens Johnson Syndrome	9	11	8	12
Toxic Epidermal Necrolysis	2	8	6	4
Total	11 (36.7 %)	19 (63.3 %)	14 (46.6 %)	16 (53.3 %)

Table 2: *Drug Groups with Clinical Patterns of Cutaneous Drug Reactions*

Drug Reaction	Type of Drug					
	Antibiotics	NSAIDs	Anti-Epileptic Drugs	Anti-Hypertensive Drugs	Miscellaneous Drugs	Total
Stevens Johnson Syndrome	8	4	1	1	6	20
Toxic Epidermal Necrolysis	5	0	0	1	4	10
Total	13	4	1	2	10	30

DISCUSSION

Cutaneous Adverse Drug Reactions (CADRs) significantly diminish the quality of life, with repeated prolonged hospital admissions and increased morbidity.[8] A frequent reason cited for the discontinuation of treatment without completing the therapeutic course is the development of a skin eruption.[9] No drug should be prescribed without warning of its potential adverse effects, especially serious CADRs, as they are a common cause for litigation.

Our study highlighted the fact that SJS and TEN were quite common among CADRs presenting to dermatologist. SJS and TEN constituted 14.3% of total CADRs in our study. A similar Study from Chandigarh also reported almost similar results (14.4%). The frequency of CADRs including SJS and TEN was more in patients older than 25 years as compared to younger patients. This conforms to two other studies which also observed elderly being the more commonly affected.[10,11] Reason could be due to the multiple drug intake by the elderly for concomitant diseases as well as increased tendency for drug interactions because of decreased functioning of various systems of the body.

In this study, antibiotics were responsible for majority of cases of SJS (40 %) and TEN (50 %), followed by miscellaneous drugs e.g. oral contraceptives, allopurinol, corticosteroids (32.4%) and then NSAIDs (23.3 %).

In one previous study, the largest number of cutaneous adverse drug reactions were associated with the use of antimicrobial agents (48%), followed by NSAIDs (24 %), and anti-hypertensive drugs (8 %). 12A large study done in Italy also reported that anti-microbial agents were the most common cause of CADRs.[13]

The main limitation of our study was that the serum levels of the culprit drugs or drug re-challenge tests were not done to confirm the diagnosis. Long-term follow-up could not be done as many patients didn't turn-up once they got cured.

It is extremely important that clinicians have comprehensive knowledge of suspected cutaneous adverse drug reactions especially the life threatening ones like SJS and TEN. Along with this, early reporting and prevention of such CADRs by physicians will definitely reduce their frequency and severity. Physicians should update themselves regarding new cutaneous adverse drug reaction patterns and their management as new drugs are being added regularly. Patient should always be educated about the ill effects of the drug prescribed and advised to stop the drug once any untoward effect of prescribed medicine is noticed and report to the physician as early as possible.

CONCLUSION

The occurrence of severe cutaneous adverse drug reaction SJS and TEN is quite common (14.3%) among patients of CADRs

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HEALING OF TIBIAL NONUNIONS TREATED WITH NA EXTERNAL FIXATORS: ITS RATE, TYPES, TIME, AND RELATED FACTORS IN PATIENTS MANAGED AT MAYO HOSPITAL, LAHORE, PAKISTAN

Syed Asif Ali[a], Usman Zafar Dar[a], Tayyab Shoib[a], Salma Batool[b], Farrukh Siddique[b], Faridoon Siddique[b]

[a]Gujranwala Medical College/Teaching Hospital, Gujranwala, Pakistan
[b]Shalamar Hospital, Lahore, Pakistan

Abstract

Objective: To determine the rate of healing of tibial nonunions treated with NA external fixator, types and time of healing, and factors affecting this healing process in our patients at Mayo hospital, Lahore, Pakistan.

Methodology: This was a retrospective cohort analysis conducted in the Department of Orthopedics, Mayo hospital, Lahore. The data of the tibial nonunion patients of all age groups who followed from July 2002 to June 2012, was included. Age of patients and healing time were the quantitative variables, while gender, childhood age group, side of the fracture, anatomic location of tibial lesion, type of fracture in term of presence of skin lesion, presence of any comorbid systemic disease, mode of reduction of fracture, bone grafting, and complications of NA external fixator were the qualitative variables.

Results: Out of total of 144 patients, 91.7% achieved healing; 6.3% (n=9) patients healed via primary healing while 85.4% (n=123) patients via secondary healing. The healing time ranged from 80-1108 days, with a mean value of 277.73 + 193.13 days. 71.4% (15 out of 21) patients with proximal tibial fracture & 95.1% (117 out of 123) patients with middle or distal tibial fracture achieved healing. The association between anatomic location of tibial lesion and healing of nonunion was statistically significant (p = 0.002). However, healing of tibial nonunion has no statistically significant association with gender (p=0.363), childhood age group(p=0.113), side of the fracture (p=0.754), type of fracture (p=0.714), comorbid systemic disease (p=0.541), mode of reduction of fracture (p=0.109), bone grafting (p=0.123), and complications of external fixator (p=0.541).

Conclusion: Tibial nonunions patients treated with NA external fixator had excellent healing rate and acceptable healing time in our studied population. Majority patients healed via secondary bone healing and only few had primary bone healing. Healing rate was significantly more for middle / distal tibial lesions as compared to proximal lesions. Gender, childhood age group, side of the fracture, skin lesion, coexisting systemic disease, mode of reduction of fracture, bone grafting, and complications of external fixator had no impact on the healing of tibial nonunion.

Keywords: Tibial nonunions, External fixation, Healing rate, Healing time, Types of bone healing

Tibial non-union is defined as a fracture that has not united without additional intervention within 6-9 months.[1] Its incidence ranges between 8-13%[1,2,3] It occurs most commonly due to poor blood supply and inadequate fracture stabilization.[4] Known risk factors for nonunion include smoking,[5] male gender,[6] open fracture,[7] NSAIDs use,[8] and many more.[6,9] Tibial nonunion is managed by surgical treatment[10] and bone stimulation.[11] Surgical options include removal of scar tissue and internal or external fixation with or without bone grafting.[10] Despite good management, treatment failure rate of tibial non-union have been reported upto 20%.[12] External Fixators are frequently used in the management of tibial non-unions, especially infected non-unions.[10] In external fixation, fractured bone is stabilized at a distance from the injury or operative focus using metal pins, clamps and external bar.[13]

Naseer Awais (NA) external fixator was invented by Professor Muhammad Awais in 1980 and is common in practice in our hospitals. In literature about tibial nonunion, healing rate was 86.2%[14] and median healing time was 126 days.[15] Bone healing can be primary or secondary. Primary bone healing[16] occurs when bony fragments are rigidly fixed together & there is no callus formation. While secondary bone healing[17] occurs when there is small amount of motion in between fracture fragments, which results soft callus formation. The objective of our study is to determine the rate of healing of tibial nonunion treated with NA external fixators, types and time of healing, and factors affecting this healing process in our patients at Mayo hospital, Lahore, Pakistan.

METHODS

This retrospective cohort analysis was conducted on the data of the patients in the Department of Orthopedics, Mayo hospital, Lahore. All the patients suffering non-union tibia fracture of all age groups who followed from July 2002 to June 2012 were included in this study. Their initial treatment was external fixator, nail, or plate and non-union was defined by non-healing at 9 months of management of the fracture.1 Then, they were managed using NA external fixators and were followed till healing or persistent nonunion was declared. The age of the patients was categorized into childhood if < 13 years, adolescence if 13-18 years, young adults if 19-44 years, middle aged adults if 45-65 years, and older adults if >65 years.[16,17] Gender of the patients, gender, side of the fracture, anatomic location of tibial lesion, skin lesion, comorbid systemic disease, mode of reduction of fracture, bone grafting, and complications of NA external fixator were also noted. After treating these tibial non-union patients, type of bone healing and time of healing in days were also noted. Type of bone healing was categorized into primary healing, secondary (periosteal) healing. Healing time was defined in days calculated since the time NA external fixator was applied till healing was achieved. Statistical analysis was completed using the Statistical Package for Social Science (SPSS), version 25. Age of the patients and healing time were the quantitative variables, while gender, childhood age group, side of the fracture, anatomic location of tibial lesion, type of fracture in term of skin lesion, coexisting systemic disease, mode of reduction of fracture, bone grafting, and complications of external fixator were the qualitative variables. Frequencies and percentages were computed for qualitative variables, while mean and standard deviation were calculated for quantitative variables. The chi-square test was applied on the data and p-values were considered as statistically significant if < 0.05. Odds ratios with 95% confidence interval for predictors of healing of tibial nonunion were also calculated.

RESULTS

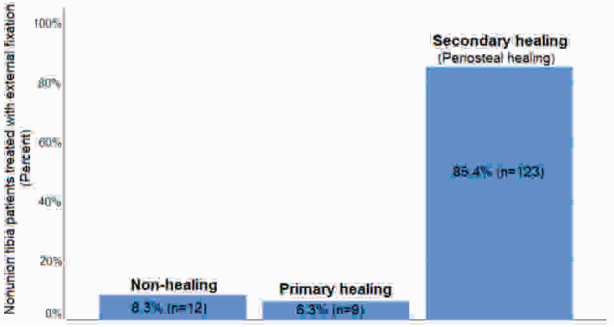
Out of 144 tibial non-union patients who were treated with NA external fixator, 91.7% (n=132) achieved healing; 6.3% (n=9) patients healed via primary healing while 85.4% (n=123) patients via secondary healing (periosteal healing). However, 8.3% (n=12) patients could not be healed with external fixation after a prolonged follow up (Picture 1). The healing time of non-union patients ranged from 80-1108 days, with a mean value of 277.73 + 193.13 days (Picture 2). Amongst tibial non-union patients managed with external fixation, 90.5% (114 out of 126) males & 100% (18 out of 18) females achieved healing. The association between gender and healing of tibial nonunion was statistically insignificant (p = 0.363). While considering different age groups, amongst childhood age group 80% (12 out of 15) patients achieved healing while amongst age groups other than childhood, 93% (120 out of 129) patients achieved healing. The association between age groups and healing of tibial nonunion was statistically insignificant (p = 0.113). 90.9% (90 out of 99) patients with tibial nonunion of right side and 93.3% (42 out of 45) patients with tibial nonunion of left side achieved healing. The association between side involved in fracture and healing of tibial nonunion was statistically insignificant (p = 0.754). 71.4% (15 out of 21) patients with

proximal tibial fracture & 95.1% (117 out of 123) patients middle or distal tibial fracture achieved healing. The association between anatomic location of tibial lesion and healing of tibial nonunion was statistically significant (p = 0.002). 92.1% (105 out of 114) patients with open tibial fractur and 90% (27 out of 30) patients with closed tibial fractur achieved healing. The association between coexisting skin lesion and healing of tibial nonunion was statistically insignificant (p = 0.109). 89.5% (51 out of 57) patients with comorbid systemic disease & 93.1% (81 out of 87) patients without comorbid disease achieved healing. The association between presence of comorbid disease and healing of tibial nonunion was statistically insignificant (p = 0.541). While considering the mode of reduction of tibia fracture, 94.1% (96 out of 102) of patients with open reduction & 85.7% (36 out of 42) of patients with close reduction achieved healing. The association between mode of reduction and healing of tibial nonunion was statistically insignificant (p = 0.109). Similarly, healing was achieved in 100% (27 out of 27) patients in which bone grafting was performed. Healing was also achieved in 89.7% (105 out of 117) patients in which bone grafting was not performed. The association between bone grafting and healing of tibial nonunion was statistically insignificant (p = 0.123). 93.1% (81 out of 89) patients in which complications of NA external fixator occurred and 89.5% (51 out of 57) patients in which complications of NA external fixator did not occur, achieved healing. The association between complications of NA external fixator and healing of tibial nonunion was statistically insignificant (p = 0.541) (Table 1).

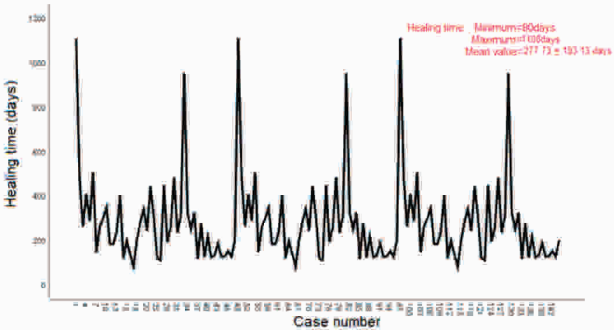
Table 1: *Statistical Correlation between healing of Tibial Nonunion and Multiple Predictors/ Factors in Patients Treated with External Fixation (n = 144)*

Predictors / Factors	Healing of tibial nonunion		Total	p-value	Odd ratio with 95% Confidence interval
	Achieved	Not-achieved			
Gender:					
Male	114 (90.5%)	12 (9.5%)	126	0.363	1.105 (1.044 - 1.170)
Female	18 (100%)	0 (0%)	18		
Childhood (Age group):					
Yes	12 (80%)	3 (20%)	15	0.113	3.333 (0.794 – 14.000)
No	120 (93%)	9 (7%)	129		
Side of lesion:					
Right	90 (90.9%)	9 (9.1%)	99	0.754	0.714 (0.184 – 2.775)
Left	42 (93.3%)	3 (6.9%)	45		
Anatomic location of tibial lesion:					
Proximal	15 (71.4%)	6 (28.6%)	21	0.002	0.128 (0.037 – 0.449)
Middle or distal	117 (95.1%)	6 (4.9%)	123		
Type of fracture:					
Open fracture	105 (92.1%)	9 (7.9%)	114	0.714	1.296 (0.328 –5.119)
Close fracture	27 (90.0%)	3 (10.0%)	30		
Co-existing systemic disease:					
Yes	51 (89.1%)	6 (10.5%)	57	0.541	0.630 (0.193 - 2.058)
No	81 (93.1%)	6 (6.9%)	87		
Mode of reduction:					
Open	96 (94.1%)	6 (5.9%)	102	0.109	2.667 (0.807 – 8.806)
Closed	36 (85.7%)	6 (14.3%)	42		
Bone grafting:					
Yes	27 (100%)	0 (0%)	27	0.123	0.897 (0.844 – 0.954)
No	105 (89.7%)	12 (10.3%)	117		
Complications of External fixator:					
Yes	81 (93.1%)	6 (6.9%)	87	0.541	1.588 (0.486 – 5.192)
No	51 (89.5%)	6 (10.5%)	57		

Picture 1: Type of bone healing achieved in non-union tibia patients treated with NA external fixator (n=144)



Picture 2: Healing time of non-union tibia patients treated with NA external fixator (n=144)



DISCUSSION

Robert Zura et al[14] found a healing rate of 86.2% in a cohort analysis of 767 tibial non-union patients while in our study, 91.7% (n=132) tibial nonunion patients achieved healing. Daily Hannah L15 reviewed 1003 tibial nonunion patients and median time to healing was 126 days. Similarly, Jae Ho Cho et al[18] and Drosos et al[19] found the mean bone union time of 143 days and 181 days respectively. In our study, the mean healing time was 277.73 days. More healing time resulting more healing rate in our data is suggestive that wait and see with tolerance in cases of tibial nonunion managed with NA external fixators is a better policy, giving good end yield. In 212 tibial fracture patients, Michail Beltsios and his colleagues[20] found that primary healing occurred in 4.7% (n=10) patients, however in our data primary healing was seen in 6.3% tibial nonunion patients. Secondary healing is superior to primary healing because risk of refracture is relatively less with secondary healing.[16] It is suggested that rigid fixation should be avoided in our patients so that some micromotion[16] should be availed for callus formation. In our study, middle or distal tibial nonunions healed significantly more than proximal tibial nonunions (p = 0.002). International literature is reverse telling where multiple review said that metaphyseal fractures heal faster than diaphyseal i.e. shaft fractures.[21] In our population, gender, childhood age group, side of the fracture, type of fracture in term of skin lesion, comorbid systemic disease, mode of reduction of fracture, bone grafting, and complications of external fixator has no impact on the healing of tibial nonunion. However, vast studies with a large sample size are required to elaborate these findings.

CONCLUSION

Tibial nonunions patients treated with NA external fixator had excellent healing rate and acceptable healing time in our studied population. Majority patients healed via secondary bone healing and only few had primary bone healing. Healing rate was significantly more for middle / distal tibial lesions as compared to proximal lesions. Gender, childhood age group, side of the fracture, skin lesion, coexisting systemic disease, mode of reduction of fracture, bone grafting, and complications of external fixator had no impact on the healing of tibial nonunion.

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RELATATIVE QUANTIFICATION OF INTERCELLULAR ADHESION MOLECULE-1 (ICAM-1) AND VASCULAR ENDOTHELIAL GROWTH FACTOR-C (VEGF-C) IN COLORECTAL CARCINOMA

Mujahid Habib, Rakhshindah Bajwa, Ahsan Sattar Sheikh, Ambereen Anwar, Shahid Habib Ansari.

Pakistan

Abstract

Background: Colorectal cancer (CRC) is the third most common cancer in the world and leading cause of death in approximately 50% of CRC patients. In Pakistan, CRC ranks 6th carcinoma among the ten most prevailing carcinomas in men with an incidence rate of 5.7%. In females, it is 9th most prevailing carcinoma with an incidence rate of 5.0%.

Objective: The objective of study was to find relationship between adhesion molecule ICAM-1 and angiogenic factor VEGF-c in CRC.

Method: This study was prospective in nature and 55 fresh clinically diagnosed colorectal tissues were taken in which 45 cases were diagnosed histopathologically as colorectal carcinoma having different stages. Reverse Transcriptase Polymerized Chain Reaction was done with LUX Primers and ICAM-1 and VEGF-c gene expression was observed.

Results: Out of 55 clinically diagnosed cases, ten cases had no carcinoma histopathologically and showed slight gene expression for ICAM-1 and VEGF-c (Mean Ct value 40.32 and 39.91 respectively) and these samples were taken as control. There were 32 (71.1%) male and 13 (28.9%) female patients. The mean age of patients was 48.31+15.60 years. All 45 cases of CRC showed ICAM-1 and VEGF-c gene expression and VEGF-c is more as compared to ICAM-1 in the respective group. But statistically data shows ICAM-1 and VEGF-c both were increased. They were more increased in early stage as compared to later stages.

Conclusion: It is concluded that ICAM-1 and VEGF-c gene expression is highest in early clinicopathological stage and less in later stages. Owing to this reason, ICAM-1 and VEGF-c should be used as biomarkers for the prognosis and staging of colorectal carcinoma.

Colorectal carcinoma is the 3rd most frequently diagnosed carcinoma globally. Worldwide burden is almost 1.4 million new cases seen in 2012 (Pietrzyk, 2016). It is a leading cause of mortality in half of the patients with CRC (Ferlay et al., 2013). At present, very limited number of national cancer registry centres/program exists in Pakistan. Only retrospective analysis of these reported cancer patients is being done since 2000 to 2008. In this study, 6.9% GIT tumours occur in males whereas 4.9% occur in females (Hanif et al., 2009).

The carcinoma related molecular and cellular markers could be categorized into 4 groups: 1) Diagnostic markers which are utilized for early recognition and risk stratification. 2) Investigative markers, provide a symptom of the possible disease progression. 3) Prognostic markers, envisage therapy response. 4) Surveillance markers, utilized to observe reappearance of disease (Aghagolzadeh & Radpour, 2016).

The adhesion and later communication between host and carcinoma cells engage a dynamic partaking of CAM (cell adhesion molecules) which give shared adherence and contact of these cells with one another and with extracellular cell matrix (ECM) (Tung et al., 2012). The cell adhesion molecules family comprises immunoglobulinlike molecules ICAM-1 (intercellular adhesion molecule-1) and VCAM-1 (vascular cell adhesion molecule-1) (Tao et al., 2012). Also the ICAM-1 referred

to CD45, is 80-114 kDa inducible surface glycoprotein being a member of immunoglobulin super family (Huang et al., 2004). ICAM- 1 is located on surface of the leukocytes or on endothelial cells and its manifestation is controlled by numerous cytokines, for example TNF-a (Tumor Necrosis Factor-a), INF-g (Interferon- g), IL-2 (Interleukin-2) and IL-6 (Interleukin-6), which may be valuable for anticancer response (Schwaeble et al., 1993).

Intercellular Adhesion Molecule-1 expression is mostly raised in tumors and this is hypothesized that expression in tumors cell could have a useful importance by enhancing the invasiveness / migration of cells (Wang et al., 2013). Angiogenesis, which is a physiological procedure involving new blood vessels growth from the pre-exist vessels and plays a significant role in growth and development of tumor. Tumour growth is probable owing to new blood vessels formation (Asem et al., 2013). Targeting of the tumour angiogenesis is demonstrated to be a useful technique to repress the growth of tumour and then metastasis (de la Torre et al., 2005).

VEGF (vascular endothelial growth factor) is a best- characterized and most significant angiogenic gene marker (Kushlinskii et al., 2014). It is from the super family of platelet-derived growth factor (Ye et al., 2013). Vascular endothelial growth factor strongly boosts vascular porously and encourages new blood vessels formation by motivating endothelial cells to divide and migrate (Tsai et al., 2013). Uncountable citations suggest that VEGF is over-expressed in major proportion of solid carcinomas of human (Morita et al., 2013). VEGF family members include VEGF-A, -B, -C, -D, -E, and PlGF (placental growth factor) (Jang et al., 2013). Importantly, the VEGF amount expressed by carcinoma cells is found to associate with weak diagnosis in several kinds of tumours, comprising cancers of kidney, breast, ovary, cervix, brain, esophagus, bladder, prostate, thyroid, in osteoid, pediatric tumours and soft tissue sarcomas (Zhou et al., 2011).

A few researches suggested that VEGF gene expression is associated with metastasis and poor diagnosis (Ferroni et al., 2005). Furthermore, another gene marker, similar to ICAM-1 is also shown to possess angiogenic activity. The two markers mechanistically differ in the formation and progression of tumor/cancer growth (Dymicka-Piekarska et al., 2012). The aims and objectives of this research was to assess the relationship between the adhesion molecules ICAM-1 and the main proangiogenic factor VEGF-c; involvement of ICAM-1 and VEGF-c in colorectal cancer staging; and use of ICAM-1 and VEGF-c as prognostic markers in colorectal carcinoma.

METHODS

Fifty Five specimens were collected in which forty five specimens had CRC and ten specimens were having normal histology. The cases were collected from Surgical Departments of Lahore General Hospital Lahore, Mayo Hospital Lahore, Ittefaq Hospital Lahore and Nishtar Hospital Multan. Reverse Transcriptase Polymerized Chain Reaction (RT. PCR) was done with LUX Primers and ICAM-1 and VEGF-c gene expression was observed. Results were analyzed on SPSS (Version 23.0) on the amplification profile for significance by ANOVA and correlations with other variants.

RESULTS

This study included 55 clinically diagnosed cases of colorectal carcinoma. This study was prospective in nature. Out of 55 cases, 45 cases were histopathologically confirmed as colorectal carcinoma whereas remaining 10 had no carcinoma. All 55 cases were processed for polymerized chain reaction in which 10 cases which had no carcinoma were used as control.

Among histopathologically diagnosed patients, 21 (46.6%) had grade-1 adenocarcinoma and 17 (37.8%) had grade-2 adenocarcinoma while 7 (15.6%) patients had grade-3 adenocarcinoma. The tumor size in the present study was assessed and found that 2 (4.4%) patients had T1 carcinoma, 8 (17.8%) had T2 carcinoma and majority 32 (71.1%)

had T3 carcinoma while 3 (6.7%) patients had T4 carcinoma according to American Joint Committee on Cancer (AJCC) classification of colorectal carcinoma.

On PCR, Cycle threshold (Ct) value was inversely proportional to the gene expression with stage of tumour. The mean Ct value of ICAM-1 of 10 samples was 40.32, T1 had mean Ct value 33.21, T2 had mean Ct value 33.45, T3 had mean Ct value 29.11 and lastly T4 had mean Ct value 25.19. As far as VEGF-c is concerned, 10 patients without cancer had mean Ct value of 39.91, T1 had Ct value 32.45, T2 had mean Ct value 32.94, T3 had mean Ct value 28.47 and lastly T4 had mean Ct value 23.04.

The results of both parameters showed that gene expression is more expressed in colorectal carcinoma as compared to samples without carcinoma. Moreover, as the stage of tumour increased, the ICAM-1 and VEGF-c gene expression also increased. When we compared both parameters, VEGF-c showed more intense gene expression as compared to ICAM-1 in respective tumour stage. ICAM- 1 gene expression gave Ct value of 25.19 in T4 stage whereas VEGF-c gave Ct value of 23.04 for the same group of tumours. In short, this study showed that VEGF-c is more specific than ICAM-1.

Table 1: *Distribution of Age*

S.No.	Age (years)	Number of patients (n)	Mean+ SD
1.	19 - 25	4	21.5 ± 1.732
2.	25.1 - 31	1	31.0 ± -*
3.	31.1 - 37	6	33.6 ± 1.505
4.	37.1 - 43	6	39.8±1.329
5.	43.1 - 49	2	45.0±0.000
6.	49.1 - 55	10	52.1 ±2.183
7.	55.1 - 61	7	59.5± 0.786
8.	61.1 - 67	2	65.0± 0.000
9.	67.1 - 73	2	69.0 ±1.414
10.	73.1 - 79	4	75.0 ± 0.000
11.	>79	1	92.0±-*
	Total	45	

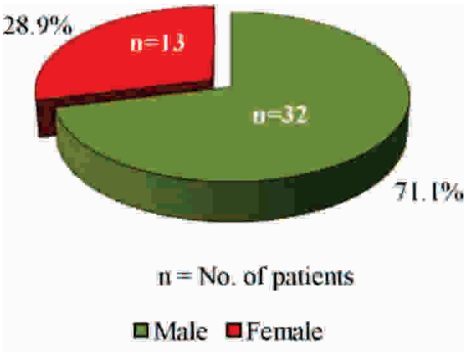

Figure-1: *Distribution of Gender*

Table 2: *Histopathological Grades of Patients with Colorectal Carcinoma*

Histopathological Diagnosis	Frequency	Percentage (%)
GI	21	46.6
GII	17	37.8
GIII	7	15.6
Total	45	100.0

Table 3: *Tumour Size of Patients with Colorectal Carcinoma according to AJCC*

AJCC Stage	Frequency	Percentage (%)
T1	2	4.4
T2	8	17.8
T3	32	71.1
T4	3	6.7
Total	45	100.0

Table 4: *Distribution of Ct Values of ICAM-1 in Colorectal Carcinoma*

AJCC Stage	Mean (Ct value)	N	Standard Error of Mean (SEM)
T1	33.21	2	0.09
T2	33.54	8	0.13
T3	29.11	32	0.11
T4	25.19	3	0.20

Table 5: *Distribution of Ct Values of VEGF-c in Different Stages of Colorectal Carcinoma*

AJCC Stage	Mean (Ct value)	N	Standard Error of Mean (SEM)
T1	32.45	2	0.24
T2	32.94	8	0.21
T3	28.47	32	0.10
T4	23.04	3	0.09

Table 6: *Analysis of Variance between ICAM-1 and Different Variables*

		Sum of Squares	Df	Mean Square	F	Sig.
Age	Between Groups	7593.978	32	237.312	0.635	
	Within Groups	4485.667	12	373.806		0.851
	Total	12079.644	44			
Gender	Between Groups	5.828	32	0.182	0.640	
	Within Groups	3.417	12	0.285		0.847
	Total	9.244	44			
VEGF-c	Between Groups	276.529	32	8.642	210.032	
	Within Groups	.494	12	0.041		0.000
	Total	277.022	44			
Tumor size	Between Groups	17.200	32	0.538	0.0	
	Within Groups	0.000	12	0.000		0.000
	Total	17.200	44			
Grade	Between Groups	16.394	32	0.512	0.848	0.662
	Within Groups	7.250	12	0.604		
Total		23.644	44			

Table 7: *Analysis of Variance between VEGF-c and Different Variables*

		Sum of Squares	Df	Mean Square	F	Sig.
Age	Between Groups	11091.811	38	291.890	1.773	
	Within Groups	987.833	6	164.639		0.244
	Total	12079.644	44			
Gender	Between Groups	7.911	38	0.208	0.937	
	Within Groups	1.333	6	0.222		0.601
	Total	9.244	44			
[CAM-1	Between Groups	228.975	38	6.026	121.295	
	Within Groups	0.298	6	0.050		0.000
	Total	229.273	44			
Tumor size	Between Groups	17.200	38	0453	0.0	
	Within Groups	0.000	6	0.000		0.000
	Total	17.200	44			
Grade	Between Groups	20.644	38	0.543	1.087	
	Within Groups	3.000	6	0.500		0.509
	Total	23.644	44			

DISCUSSION

This study consisted of 45 cases of colorectal carcinoma which were diagnosed histopathologically. These samples were taken fresh and RT-PCR was applied to see ICAM-1 and VEGF-c gene expression along with 10 samples which had no carcinoma.

As far as gender is concerned, 32 cases (71.1 %) were male patients and 13 cases (28.9 %) were female patients. 23 (51.0 %) males and 9(20.1%) females were found to lie in stage T3 according to tumour size.

The age of the patients ranged from 2nd to 9th decade, most of the patients were in 5th decade. The statistical analysis shows that as the age increases, ICAM-1 and VEGF-c gene expression decreases. This study evaluated that there is shift of age group from older age to relative younger age group. Previously it was evaluated that CRC is the disease of old age as studied by Whiffin and coworkers (2014) and concluded in their study that CRC risks increased with higher ages.

Our study is compatible with the study conducted by Amini and coworkers (2013). They carried a study at Civil Hospital Karachi on occurrence of colorectal carcinoma in younger population. 23 patients of CRC were taken in which 13 (56.52%) were males with mean age 42.3+16 years while females were 10 (43.47%) with a mean age of 40+18 years. 12 (52.17%) patients were below 40 years whereas remaining 11 (47.83%) patients were above 40 years. The study concluded two spheres: males were affected more and CRC had been increasingly becoming more common in relatively younger population. This is due to change in dietary habits, lifestyle related factors and improved diagnostic tools.

The statistical data also shows that all samples show gene expression for ICAM-1 and VEGF-c even in samples without colorectal carcinoma. For normal tissues mean Ct values of ICAM-1 and VEGF-c are 40.32 and 39.91 respectively. When Ct value decreases, the gene expression of ICAM-1 and

VEGF-c increases. It means the Ct value is inversely proportion to gene expression.

The present study is compatible with study conducted by Kang and coworkers (2005). They investigated the correlation between serum soluble intercellular adhesion molecule-1 and clinicopathological features. 56 patients of colorectal carcinoma were taken along with 25 control patients. The results showed that poorly differentiated colorectal carcinoma had a higher level of serum ICAM-1 than those with differentiated carcinoma (736.49±121.97 ug/L vs 410.23±67.97 ug/L, P < 0.001). The study concluded that serum ICAM-1 levels were found to be related to tumour presence.

The present study expressed mean Ct value of T_1 (32.45) and T_4 (23.04) which is compatible with the study conducted by Akagi (2000) showing relationship between expression of VEGF-c and clinicopathological features in patients with colorectal cancer. The expression of VEGF-c in the 99 primary tumours and 18 metastatic lymph nodes from colorectal cancer patients was examined immunohistochemically. To verify VEGF-c mRNA expression, reverse transcriptase-polymerase chain reaction (RT-PCR) was carried out. Results showed that survival time was shorter for VEGF-c positive groups than for VEGF-c negative ones (p = 0.0032).

Our study is compatible (-0.905**) with the study conducted by Szajewski and coworkers (2015) who evaluated the relationships between expression of VEGF-c and vessel density in patients with locally advanced (pT3 - T4) colorectal carcinoma.104 specimens of primary, locally advanced (pT3-4) colon adenocarcinoma were taken. IHC was performed. The study concluded that expression of VEGF-c is more intense in T1 tumour size as compared to T3 and T4 (p = 0.03). Moreover, expression of VEGF-c was more intense in T1 tumour size.

The reason is that in T1 tumour size, no necrosis was seen and there was well developed vascular channels in the periphery of tumour as well as centre of the tumour.

The present study is compatible with the animal study conducted by Yonemura and coworkers (2005). They studied the molecular mechanisms of Lymphangiogenesis induced by VEGF-c and VEGF-D in gastric carcinoma. RT-PCR and Western Blot were conducted. Results showed that the lymphatic vessels in VEGF-c (52.0±9.5) and VEGF-d (16.4±0.6) were highly significant than that of control (4.0±1.4). It is concluded that VEGF-c and VEGF-d create neoformation of lymphatic vessels in experimental gastric tumour. The reason is that VEGF-c induced lymphangiogenesis by activating VEGF receptor (VEGFR- 3).The newly developed lymphatic vessels were developed not in the periphery but also centre of the transfected area.

The present study is not compatible (-0.905**) with the study conducted by Ichikura and his team (2001). They studied on prognostic importance of VEGF and VEGF-c expression in gastric carcinoma. 76 cases were taken and IHC for VEGF and VEGF-c was applied. The results showed that VEGF and VEGF-c showed immunoreactivity in 39 % and 45% patients respectively . It was concluded that VEGF-cstimulate the tumour progression. But the present study showed that in T4, the intensity of gene expression was not so intense as that of T1 due to development of necrosis in central area of tumour which caused damage to blood vessels. In short, ICAM-1 and VEGF-c both are good biomarkers for the prognosis of colorectal carcinoma.

CONCLUSION

Colorectal carcinoma is becoming disease of middle age in Pakistan. Out of eleven age groups, four age groups ranging from 31 years to 55 years having 34 patients and remaining 21 patients lie in 7 age groups. It effects more males than females. Statistical data shows that ICAM-1 and VEGF-c gene expression is present in all CRC patients. But VEGF-c gene expression is higher in early stage and less in later stages, whereas ICAM-1 gene expression increases as the grade level increases they should be applied along with conventional histopathology for confirmation of diagnosis. These two markers can be applied for simultaneous quantification. In addition, ICAM-1 and VEGF-c should be used as prognostic markers.

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