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Editorial

Increasing Incidence of Depression

Mohsin Masud Jan

Editor

Depression is becoming a common global issue, especially in developing countries. “Almost one million lives are lost yearly due to suicide deaths every day. In fact, depression is the leading cause of disease burden for women in both high income and low income population.” A depressive disorder is an illness that involves the body, mood, and thoughts. It affects the way person eats and sleeps, the way one feels about oneself, and the way one thinks about things. Without treatment, symptoms can last for weeks, months, or years. Appropriate treatment, however, can help most of the people suffering from it.

Depression accounts for 6 per cent of all mental illnesses in Pakistan and the rate is increasing due to factors like economic loss, insecurity, political uncertainty, unemployment, stressful working conditions, gender discrimination and disruption of the social settings.

According to the health experts depression affects people in all communities across the world. Today, it is estimated to affect 350 million people worldwide. It is estimated Depression and anxiety disorders cost the global economy \$ 1 trillion each year in lost productivity.

This disorder often starts at a young age; they reduce people's functioning and often are recurring. For these reasons, depression is the

leading cause of disability worldwide in terms of total year lost due to disability.

In developing countries, maternal depression may be a risk factor for poor growth in young children. This risk factor could mean low-income countries may have a substantial influence on growth during childhood, with the effects of dispersion, affecting not only this generation but also the next.

Spouses of heart attack victims are at high risk of anxiety, depression. It is observed that a heart attack is a bigger psychological blow to the victim's wife or husband than any other illness and flags up the need for providing them with care and attention. It is observed that more than three times the number of people whose spouses died from a heart attack was using antidepressant in the year after the event compared with the year before. The rates of depression were significantly higher after the event in the fatal heart attack group.

World Mental Health Day is observed on October 10 every year, with the overall objective of raising awareness of mental health issues around the world and mobilizing efforts in support of mental health. The day provides an opportunity for all stakeholders working on mental health issue to talk about their work, and what more needs to be done to make mental health care reality for people worldwide.

Clinical Profile of Diabetes Mellitus Type 1 in Pediatric Patients Admitted in PMCH Nawabshah

Ali Akbar Siyal¹, Juverya Naqvi¹ and Tabinda Taqi²

ABSTRACT

Objective: To look at the frequency of children having type 1 diabetes mellitus and their clinical profile.

Study Design: Observational study

Place and Duration of Study: This study was conducted at the Pediatric Ward, Peoples Medical College Hospital, Nawabshah from November 2016 to October 2017.

Materials and Methods: Files of patients with either diagnosis at admission as diabetes mellitus type 1 or later diagnosed as diabetes mellitus type 1 during hospital stay were collected and data was retrieved regarding gender, age, number of days in hospital, presentation, type of insulin used, and acute complications developed if any.

Results: Total patients admitted in ward 10554 from November 2016 to October 2017, age ranging from 1 year to 15 years. Out of these 10554, 57 patients were treated as having type 1 diabetes mellitus, with a mean age of 7.5 years, the female were 61%. Mode of presentation was Diabetic ketoacidosis (DKA) in 50 patients, and 7 patients were diagnosed incidentally during stay at hospital for some other disease. 1 Patient developed cerebral edema during DKA management, 3 patients developed episodes of hypoglycemia, rest of the patients were discharged without complication.

Conclusion: Diabetes mellitus type 1 in recent years has found to be an increased concern in pediatric population. In our patients it was found to be present in 0.54% admitted patients. But there is a limitation of this study that it does not depict the actual ice berg situation of this illness in our population.

Key Words: Diabetes Mellitus, Children, DKA

Citation of articles: Siyal AA, Naqvi J, Taqi T. Clinical Profile of Diabetes Mellitus Type 1 in Pediatric Patients Admitted in PMCH Nawabshah. Med Forum 2018;29(11):2-4.

INTRODUCTION

Diabetes mellitus (DM) is a chronic disease which is characterized by hyperglycemia. The main forms of the disease are differentiated by insulin deficit versus insulin resistance type 1 diabetes mellitus (T1DM) resulting from lack of insulin because of β -cell damage of pancreas. The type 2 diabetes mellitus (T2DM) is a consequence of insulin resistance that occurs in skeletal muscle, liver, and adipose tissue, with several degrees of impairment in β -cell. T1DM is the commonest metabolic condition of endocrine system in children and adolescence, with important consequences for physical and emotional development¹. T1DM is the commonest among chronic metabolic diseases in

children, resulting in 5–10% of the total cases of Diabetes worldwide². A recent increase in non-communicable diseases (NCDs) has been observed worldwide, diabetes mellitus being one of them. Even in developing and under developed countries there has been an increase in diabetes mellitus in young adults, adolescents and children. It is documented that NCDs is killing about 15 million people yearly having age between 30 and 69 years, particularly in countries of low and lower-middle income, with almost 50% of reported premature deaths³. There are many factors that influence an individual's risk for development of diabetes mellitus including the micro and macro-environment, exercise/ activity levels, genetic propensity and many others yet to be identified risk factors. A study done at Basrah, Iraq which shows the prevalence of T1DM in 0-40 years was 87/100000⁴. Diabetes mellitus has a major social and psychological effect on children and parents, as well as has impact on health care facilities too, if left untreated it causes chronic complication and ultimately decreases the life expectancy^{5,6}. There is great variability in the initial appearance of T1DM equally in youth and adults. The disease is often acute in children, with stern symptoms of polyuria, polydipsia, and ketonemia⁷, but it is also observed that sometimes patients come with other presenting complain and then are diagnosed

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incidentally. There is a massive lack of data and research regarding the prevalence and clinical profile of T1DM in individuals less than 15 years of age in our region. This paper is just an effort in this regard to look at the clinical profile of T1DM in children admitted in pediatric unit, PMCH, Nawabshah.

MATERIALS AND METHODS

Files of patients admitted in pediatric ward PMCH Nawabshah as diabetes mellitus type 1 or later diagnosed as diabetes mellitus type 1 during hospital stay were collected and data was retrieved regarding gender, age, number of days in hospital, presentation, type of insulin used, and acute complications developed if any.

RESULTS

Total patients admitted in ward 10554 from November 2016 to October 2017, age ranging from 1 year to 15 years. Out of these 10554, 57 patients were treated as having T1DM with mean age of 7.5 years, and female patients' percentage to be higher than male patients (61% vs. 39%). Mode of presentation was Diabetic ketoacidosis (DKA) in 50 patients, and 7 patients were diagnosed incidentally during stay at hospital for some other disease. 1 Patient developed cerebral edema during DKA management, 3 patients developed episodes of hypoglycemia, rest of the patients were discharged without complication.

Table No.1: Percentage of Patients Presenting With DKA

Total Number:	DKA		Percentage
	Yes	No	
57	50	7	87.7%

■ Total Patients ■ Diabetes Mellitus Type 1

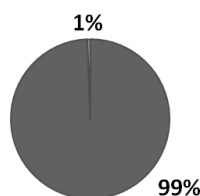


Figure No.1: Percentage of Diabetes Mellitus Type 1 in Patients Presenting to Paediatric Ward



Figure No.2: Gender Distribution of Type 1 Diabetes Mellitus

DISCUSSION

In the current study done at the pediatric unit, authors found that the prevalence/frequency of type 1 diabetes

mellitus was 57 out of 10554 admitted patients between the ages of 1 year to 15 years. Patients presenting in outpatient department are not included in our study. In a study from Bangladesh the number of patients with type 1 diabetes was 125, age ranges from 1 to 18 years⁸. Another study from Haryana state Karnal district India reports prevalence of 10.20/100,000 population, In the 5 to 16 years age group, the prevalence is 22.22/100,000, while in the 0-5 years age group, prevalence is 3.82/100,000, but this is a population based study, ours was a hospital based study with limited population⁹. In our study the mean age of presentation was 7.5 years, the youngest patient noted was 2 years old, different studies have different population age ranges, in one study from Al-Madina Saudi Arabia, mean age at presentation was 6.9 years¹⁰, but few studies match the average age with our study's mean age^{11,12}. Our study shows female predominance (61%) rather than males, studies from India and USA shows a male predominance^{9, 13}. Female predominance was seen in a study from Cyprus Greece¹⁴ in age group 10-15 years. In our study 87.71% patients presented with DKA, while 12.3% patients landed with some other complaints but were later on diagnosed with diabetes type 1 or were admitted for adjustment of insulin dose. In a large cohort study from UK, authors found that the diabetic children presenting with DKA ranged from 12.8% to 80%¹⁶, the reason of majority of patients landing in emergency department with DKA in our setup in most of the patients was poor compliance, or inappropriate management in sick days because not all patients were newly diagnosed, some of them were known case of diabetes and counseled thoroughly but they presented with DKA again and again^{12,15}. As majority of type 1 diabetes patients present with diabetic ketoacidosis, there is higher incidence of DKA related complications like cerebral edema^{16, 17}, but in our small cohort of 57 patients only 1 patient (1.7%) developed brain edema during the initial phase of treatment. Hypoglycemia is again a life threatening morbidity associated with management of diabetes mellitus type 1, as during initial management there is a high risk of hypoglycemia that develops insidiously and suddenly, our study shows that symptomatic hypoglycemia developed in 5.26% patients, in a study from USA hypoglycemia was seen in young patients especially younger than 6 years of age¹⁸. To prevent the development of DKA and DKA related complications in our setting; we have to ensure that patients and their parents/guardians understand the importance of the need for regular insulin injections with proper dose calculation and monitoring of blood glucose. This can be made sure by patient and parent education on each visit especially when they are admitted for the first time and ensure their regular follow ups. It is also important to educate them about sick-day management²⁰. There is also a strong need to spread the knowledge about

diabetes and DKA to community physicians and general population who are involved in care of diabetes mellitus in children.

CONCLUSION

The prevalence of Diabetes mellitus type 1 is increasing in younger age pediatric population. In our patients it was found to be present in 0.54% admitted patients. Most of patients develop DKA and DKA related complications.

Author's Contribution:

Concept & Design of Study: Ali Akbar Siyal
 Drafting: Juverya Naqvi
 Data Analysis: Tabinda Taqi
 Revisiting Critically: Ali Akbar Siyal, Juverya Naqvi
 Final Approval of version: Ali Akbar Siyal

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Cosmetic Outcome and Time Taken for Closure in Facial Laceration Repaired with Single Layer of Non-absorbable Monofilament Suture

Batool Urooj Rajput¹, Moiz Sadiq¹, Fahmina Buriro¹, Syed Sheeraz Ur Rahman² and Rabiya Jawed¹

ABSTRACT

Objective: To determine the cosmetic outcome of superficial facial lacerations repaired with single layer of non-absorbable monofilament suture and to observe time taken for closure and rate of infection and dehiscence.

Study Design: Prospective case series study

Place and Duration of Study: This study was conducted at the Accident and Emergency Department, Liaquat National Hospital, Karachi from 14th May 2009 to 31st January 2010.

Materials and Methods: In our study we repaired 70 superficial lacerations presented within 24 hours to accident and emergency department; with single layer of 6/0 prolene suture. We restricted the age group from 18 to 40 because young individuals are more concerned about scars.

Results: 36 patients presented within 3 hours of injury and among these 35 patients (97.2%) resulted in satisfactory outcome, 23 patients presented between 3 to 6 hours of injury and gave 95.7% satisfactory result while 11 patients presented after 6 hours and 7 patients (63.6%) gave satisfactory outcome. It indicates that repair of lacerations within 6 hours gives best outcome.

Conclusion: Single-layer closure of nongaping, minor facial lacerations, with nonabsorbable monofilament suture yield satisfactory cosmetic outcome. Cosmetic outcome improved when repaired within 6 hours of injury but there is no impact of time on rate of infection and dehiscence.

Key Words: Facial, Laceration, Scar, infection. Dehiscence, Cosmetic outcome

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INTRODUCTION

Facial laceration is one of the most common injuries presented to Accident and Emergency department.^{1,2} All facial wounds should be repaired in less than 24 hours to decrease the risk of infection and achieve the best cosmetic result.³ Although number of factors determine cosmetic outcome of facial scar like site, laceration parallel to relaxed skin tension lines etc. a variety of wound closure methods are available including steri-strip dressings, sutures,⁴ glue or staples but by far suture closure is most popular techniques.³ Nonabsorbable 6.0 monofilament or absorbable 5-0 vicryl (polyglactin) sutures can be used for interrupted or intracuticular technique.⁵

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Whether facial lacerations should be routinely closed using more than one layer of sutures is debatable.⁶ As placement of deep dermal layer is not only technically challenging but more time consuming (mean difference of 7 minutes p value 0.007), many emergency physicians do not routinely perform multilayer closure of facial laceration.⁷ Different studies have been done to compare various methods of facial laceration repair, in majority of which cosmetic outcome is similar.^{8,9,10,11} Some studies showed that monofilament suture is associated with a lower risk of infection compared with a polyfilament suture.³ In a study comparing single versus double layer closure showed infection and dehiscence rate of 0.00 in both groups (p-value 1.00).² In another study comparing absorbable versus non absorbable suture showed infection rate of 7% in absorbable group and no infection in non-absorbable group while dehiscence rate of 0.00 in both groups.⁹ While single layer closure is a simple, cheaper and less time consuming method with similar cosmetic outcome (mean difference of 1.0 with p value 0.73 on visual analogue scale), data is available internationally but no local study is done as yet.⁷ As professionals, plastic surgeons strive for the best possible cosmetic outcome when repairing facial laceration. If the results are less

than ideal, the patient unfortunately may wear a scar, like a trademark. Various methods of assessing scar quality are available and Manchester scar assessment proforma described by Beausang et al is an appropriate tool for assessing linear scars.¹²

In accident and emergency departments where facial lacerations share a large number of patients, this study may be able to help ensure that the desired cosmetic result can be achieved with single layer closure in less time while we will also be able to give rate of infection and dehiscence for comparison with international studies.

MATERIALS AND METHODS

Study was conducted in Department of Accident and Emergency at Liaquat National Hospital, Karachi from 14th May 2009 to 31st January 2010. Sample size of 70 patients of facial laceration. All patients presented to Accident and Emergency department with facial laceration fulfilling inclusion criteria were included in this study.

Inclusion criteria:

- Age group 18 to 40
- Superficial laceration
- Presented to emergency within 24 hours of injury

Exclusion criteria:

- Deep laceration
- Presented to emergency after 24 hours
- Severe contamination/ crush injury/ animal bite
- Diabetes, vascular disease, familial tendency for keloid or hypertrophic scar

Data Collection Procedure: All patients presented to Accident and Emergency department of Liaquat National Hospital with facial laceration fulfilling the inclusion criteria were included and lacerations were closed with a single layer of simple interrupted 6-0 polypropylene sutures.

To each eligible patient, procedure was explained, informed consent was taken. Lacerations were repaired by investigator with at least 2 year experience of suturing facial lacerations. Investigator measured the size and shape of the laceration, its location and orientation to relaxed skin tension line. All lacerations were examined under local anesthesia and washed with 0.9% saline solution. Time for repair was calculated by investigator, started from removal of suture from its packet and ended when outer layer of skin is completely closed. Patients were evaluated at 5 days for removal of sutures (recommended time for removal of facial stitches is 3 to 5 days), infection and dehiscence and at 3 months for cosmetic evaluation which was done by observer (a plastic surgeon with 3 years experience). All efforts were made to ensure that complete data is obtained from all candidates in the study. Manchester scar assessment proforma was used to calculate scar score. Data was collected in proforma and analyzed using SPSS version 12.

Statistical Methods: Data was analyzed with SPSS 12.0 for Windows. Categorical variables as gender, wound location, wound orientation and cosmetic outcome were presented as the percentage. Continuous variables as age, wound length and width, time taken for closure, were presented as means with standard deviations and 95 percent confidence intervals. The outcome was the long-term cosmetic appearance, as assessed by using the Manchester scar assessment proforma, time taken for closure and rate of wound infection, dehiscence. Stratification was undertaken on age, gender, site and size of wound to assess impact on outcome.

RESULTS

A total of 70 patients presented to emergency within 24 hours of injury with facial laceration were included in this study and lacerations were closed with a single layer of simple interrupted 6-0 polypropylene sutures. Most of the patients age were between 21 to 40 years of age that is 58(82.8%) as shown in Figure 1, the average age of the patients was 27.74 ± 7.34 years (95%CI: 25.99 to 29.49) similarly average time injury was 4.23 ± 2.36 hours (95%CI: 3.65 to 4.82).

Out of 70 patients, 58(82.9%) were male and 12(17.1%) were female. Characteristics of laceration of patients in length, width and shape are also presented in Table 1. Average length and width of laceration were 2.9 ± 0.96 cm (95%CI: 2.67 to 3.13) and 0.48 ± 0.23 cm (95%CI: 0.42 to 0.53) respectively. Regarding shape, 78.6% were linear and 21.4% were nonlinear.

Road traffic accident was the commonest causes of the injuries that were observed in 48(68.6%) cases followed by fall 16(22.9%), glass injury 4(5.7%), hit by fan 1(1.43%) and assault was also observed in only one case. Similarly chin, cheek, lips, eye brow was most effected location of laceration of patients which are presented in Table 2.

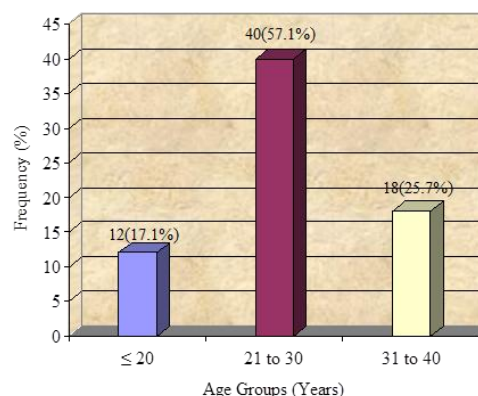


Figure No.1: Patients age with frequency

Time for repair was calculated and it started from removal of suture from its packet and ended when outer layer of skin is completely closed. The average time taken for closure was 13.47 ± 3.96 minutes (95%CI: 15.1 to 14.3). Time of closure observed in 27(38.6%)

cases was within 11 to 15 minutes, 21(30%) cases was within 6 to 10 minutes, 18(25.7%) cases was within 16 to 22 minutes and time taken for closure in 4(5.7%) cases was within 5 minutes.

Table No.1: Characteristics of laceration

Characteristics of laceration	Frequency	Percentage
Length		
➤ 1.0 to 2.0 cm	21	30%
➤ 2.1 to 3.0 cm	29	41.4%
➤ 3.1 to 4.0 cm	14	20%
➤ 4.1 to 5.0 cm	06	8.6%
Mean ± SD (95%CI)	2.9±0.96 (95%CI: 2.67 to 3.13)	
Width		
➤ ≤ 0.5 cm	59	84.3%
➤ > 0.5 cm	11	15.7%
Mean ± SD (95%CI)	0.48±0.23(95%CI:0.42 to 0.53)	
Shape		
➤ Linear	55	78.6%
➤ Non Linear	15	21.4%

Table No.2: Location of laceration of patients n=70

Location of laceration	Frequency	%age
Chin	16	22.9%
Cheek	11	15.7%
Lower and Upper Lip	11	15.7%
Eyebrow	10	11.4%
Infra Orbital	7	14.3%
Forehead	6	8.6%
Nose	5	7.1%
Upper Eyelid	3	4.3%
Lateral canthal area	1	1.4%

Table No.3: Cosmetic outcome of superficial facial lacerations with respect to characteristics of laceration

Characteristics of laceration	n	Less Satisfactory	Satisfactory
Length			
➤ 1.0 to 2.0 cm	21	1(4.8%)	20(95.2%)
➤ 2.1 to 3.0 cm	29	3(10.3%)	26(89.7%)
➤ 3.1 to 4.0 cm	14	2(14.3%)	12(85.7%)
➤ 4.1 to 5.0 cm	6	0(0%)	6(100%)
Width			
➤ ≤ 0.5 cm	59	5(8.5%)	54(91.5%)
➤ > 0.5 cm	11	1(9.1%)	10(90.9%)
Shape			
➤ Linear	55	2(3.6%)	53(96.4%)
➤ Non Linear	15	4(26.7%)	11(73.3%)
Orientation to relaxed skin tension lines: Parallel			
➤ No	17	4(23.5%)	13(76.5%)
➤ Yes	53	2(3.8%)	51(96.2%)

Infection and dehiscence infection was not observed in patients. Cosmetic outcome were measured by Manchester scar assessment score. Satisfactory (scar score 5 to 8) outcome was observed in 64(91.4%) patients while 6(8.6%) cases were less satisfactory (scar score 9 to 17)

Satisfactory scar condition was slightly higher in male (93.1%) than female (83.3%). Similarly these cosmetic outcome were analyzed according to age group, above 90% cases were found satisfactory in all age groups. One case of assault was less satisfactory and 5(10.4%) cases of road traffic accident scare outcome were less satisfactory.

Less satisfactory cosmetic outcomes were observed in patients whose time of injury was above 6 hours. Cosmetic outcome of superficial facial lacerations with respect to characteristics of laceration are also presented in Table 3.

DISCUSSION

The quality of care of acute facial lacerations can determine whether patient will receive aesthetic and functional restoration, or a disfiguring scar, with or without loss of function. The ultimate goal of facial laceration repair is to achieve a functional and aesthetically pleasing scar. This is best achieved by proper wound assessment and preparation followed by gentle tissue handling and meticulous wound closure. Proper application of plastic surgical technique is of vital importance in achievement of a minimally visible or hairline scar. In today's world where emphasis on personal appearance has increased significantly, both emergency physician and surgeons treating patients should be familiar with principles and techniques of facial soft tissue surgery to prevent subsequent cosmetic deformity or functional impairment.

Facial laceration repair is not a difficult task but an ideal repair combines gentleness with delicate tissues, thoroughness and willingness to spend time for precise closure. Using proper techniques may prevent costly scar revisions, which may never be as good as initial repair done properly. There is no single recommended method for facial laceration repair and despite of several studies on suture repair and alternate methods of facial laceration repair no major difference is found among all modalities. This indicates that general principles while repairing facial laceration are more important than method of repair. In a study of 65 patients comparing single versus double layer closure patients were randomized to closure with single layer of simple interrupted 6/0 prolene suture and a double layer of simple interrupted 6/0 prolene plus deep dermal layer of 5/0 polyglactin suture. Scar assessment was done at 90 days and author concluded that Single-layer closure of nongaping, minor facial lacerations is faster than double-layer closure. Cosmetic outcome and scar width are similar in sutured wounds whether or not deep

dermal sutures are used. In many studies comparing cosmetic outcome of facial laceration repaired with absorbable suture, non absorbable suture, tissue adhesive and steri strips concluded that there is no significant difference in cosmetic outcome in either group. Steri strips and tissue adhesive are good techniques but their use requires expertise. Non absorbable suture has advantage that we do not need to remove the sutures but generally we have seen bit more inflammatory reaction with these sutures and they are good for intradermal suture placement when it is required in closing deep wounds. In practice we have seen patients with facial lacerations repaired in some other hospitals with 2/0 silk suture, not well approximated and with wide distance from skin margins. Despite of time and resource expenditure the results are not good and such patients are then in search of re-suturing or later on presented with ugly scar. Secondly patients with facial lacerations are referred to our hospital only because of lack of plastic surgery specialties in most of the hospitals. With little changes in practices and cost, cosmetic outcome can be improved even in hospital where plastic surgical expertise is not available. Closing laceration with non absorbable prolene is easy and in majority of institutes worldwide it is done by emergency physicians and emergency theatre technicians. Only 16% facial lacerations in emergency are repaired by plastic surgeons.¹³

In our study we repaired 70 superficial lacerations presented within 24 hours to accident and emergency department; with single layer of 6/0 prolene suture and majority of our patient (91.4%) came in satisfactory result's category with acceptable cosmetic outcome. We restricted the age group from 18 to 40 because young individuals are more concerned about scars. Among these patients 57.1% were between 21 to 30 years of age indicates that younger people are more prone to trauma. There is no significant difference in cosmetic outcome among age groups.

36 patients presented within 3 hours of injury and among these 35 patients (97.2%) resulted in satisfactory outcome, 23 patients presented between 3 to 6 hours of injury and gave 95.7% satisfactory result while 11 patients presented after 6 hours and 7 patients (63.6%) gave satisfactory outcome. It indicates that repair of lacerations within 6 hours gives best outcome.

JP Shepherd a maxillofacial surgeon in one of his work on assessment of repair of facial laceration repair concluded that there is still no ideal suture for skin closure. Sutures should be easy to handle and should facilitate efficient wound closure. Secure, optimal skin/wound edge co-aptation will produce minimal tissue reaction; primary wound healing and therefore minimal scarring, particularly where infection is prevented.¹⁴

Brown et al summarized in paper on advanced laceration management that the majority of lacerations

to the face and fingertip can be managed by the emergency clinician.¹⁵

In majority of studies done on facial lacerations, the rate of infection and dehiscence is very minimal but the long-term cosmetic appearance is more important to both patients and physicians that's why we emphasize more on cosmetic outcome unlike many studies in which infection rate is used as primary outcome.

In one study by Singer A J the mean time taken for facial laceration repair with single layer was 14.7 minutes, the rate of infection and dehiscence was zero and the optimal scar score was 6.⁷

It is indicated by our study that single layer closure is as effective as any other modern technique in achieving cosmetically pleasing scar. In our study the optimal scar score and the final outcome of scar is comparable with international studies and additionally there is no wound infection and dehiscence which is also comparable with international studies where almost same results are achieved with suture closure of facial laceration in comparison with other methods. Internationally little work is done on adult population while more work is done on pediatric lacerations where emphasis is more on non-absorbable suture because suture removal is problematic in children. Unfortunately we do not have any local study done on this topic as yet.

Our study has some Limitations which need to be discussed. We have presented case series and have compared with international results. We have not done our own comparison of different modalities. But as it is first such study we may be able to do further work in our institution. We have done our study in single institute so we cannot compare with other institute's results unless we do multicenter study or same study being duplicated in other institutes also. In our study we have done scar assessment at three months and this timing is also a topic of debate. Although studies suggest that the cosmetic appearance of scars at 3 months reliably predicts 1-year outcome, one study found differences between the cosmetic appearance of wounds at 6 and 46 months.⁷ In our study we have used scoring system which has some draw backs. These types of scorings assume different scar characteristics to have the same level of importance (e.g., the score for a gross mismatch in color is assigned the same influence as that for a severe distortion). This implied weighting will not only contribute to the consistency of scores but may also lessen the sensitivity of the assessment. This is not to say that these methods are deficient; indeed, in an area that lacks general agreement regarding a premier method, and considering the broad spectrum of clinical scars that have been thus assessed, they are extremely functional tools.

CONCLUSION

Our study demonstrates that single-layer closure of nongaping, minor facial lacerations, with

nonabsorbable monofilament suture yield satisfactory cosmetic outcome. With little change in practice as selection of suture material, proper handling of tissues and proper approximation of wound edges, the outcome can be improved significantly in facial lacerations. Cosmetic outcome improved when repaired within 6 hours of injury but there is no impact of time on rate of infection and dehiscence.

Author's Contribution:

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Conflict of Interest: The study has no conflict of interest to declare by any author.

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Clinicopathological Profiles of Lymph Node Enlargement at Mayo Hospital, One Year Study

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ABSTRACT

Objective: This study aimed at evaluating the causes of lymphadenopathy and demographic distribution of patient load at Mayo Hospital, Lahore.

Study Design: Descriptive / cross-sectional study.

Place and Duration of Study: This study was conducted at the Pathology Department King Edward Medical University/ Mayo Hospital, Lahore from January 2016 to December 2016.

Materials and Methods: All lymph node biopsies were reviewed at histopathology section of Pathology Department King Edward Medical University/ Mayo Hospital, Lahore. Demographic details of patients, site of lymph node enlargement and diagnoses of lymph node biopsy were recorded on proforma. SPSS 21 and descriptive statistics were used to obtain results of age, gender, site of lymphadenopathy, residential address and diagnoses were evaluated.

Results: Total of 308 cases were included in study. Most common cause was reactive hyperplasia 218(70.8%), 56 (18.2%) showed Tuberculosis, 14 (4.5%) exhibited metastatic carcinoma, 9 (2.9%) were labeled as Atypical lymphoproliferative disorder, 6 (1.9%) were of Non-Hodgkin lymphoma, 3 (1.0%) of Hodgkin lymphoma and 2 (0.6%) of abscess. 206(66.9%) patients were from Lahore, 43 (14.0%) from Sheikhpura, 19 (6.2%) from Narowal, 17 (5.5%) from Nankana, 11(3.6%) from Okara, 7(2.3%) from Mianwali and 5 (1.6%) belonged to Bahawalnagr.

Conclusion: Reactive lymph node enlargement is most common cause of lymphadenopathy in tertiary care setup. Tuberculosis is second most common cause, seen more in females. Mayo Hospital is catering a large number of patients from cities other than Lahore. It is suggested that tertiary care services should be strengthened in areas surrounding Lahore to lower patient burden and improve health facilities at Mayo Hospital. Government hospitals should be equipped with special tests like immunomarkers and molecular techniques to precisely diagnose lymphoid malignancies.

Key Words: Atypical Lymphoproliferative disorder, Demographic, Hodgkin Lymphoma, Lymphadenopathy, Non-Hodgkin Lymphoma, Tuberculosis.

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INTRODUCTION

Lymph nodes are organized centers of immune cells that filter antigens from extracellular fluid. Lymph is ultra-filtrate of blood that passes through lymph node to get screened for antigens.¹ Lymph nodes change their size and shape according to age, location and antecedent immunological consequences. If their number, size or consistency changes they are considered abnormal and result in lymphadenopathy².

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Lymphadenopathy of inflammatory type is called lymphadenitis. Common causes of lymphadenopathy range from common cold to autoimmune diseases to cancers³. Since lymph nodes are superficially located they are available for Fine needle aspirations and biopsy for histopathological evaluation that is considered gold standard for confirmation of pathology underlying node enlargement. Reactive enlargement of lymph nodes can also occur due to internal malignancy⁴. Since many infections can mimic malignancy and vice versa, lymphadenopathy requires careful screening⁵. Clinical history of fever, weight loss, isolated/ multiple node enlargements are important signs in evaluating patients presenting with lymphadenopathy.⁶ According to World Health Organization (WHO) 8.6 million people are affected with tuberculosis (TB) worldwide⁷. Most of the reported cases are from Asia (58%) and Africa (27%), with highest incidence in India (2.4 million) and China (1.1 million). Pakistan is 5th amongst countries with highest burden of TB and 4th highest in drug resistant

Tuberculosis. 420,000 new cases occur annually in Pakistan. Still there is under-detection and under-notification of TB⁸. As no tertiary care hospital is equipped with facility of immunomarkers, lymph node biopsies that do not fulfill the criteria of completely benign or malignant features have to be labeled as atypical lymphoid disorder or atypical lymphoproliferative disorder (ALP)⁹.

MATERIALS AND METHODS

All lymph node biopsies received at Pathology department of King Edward Medical University (KEMU) were collected from January 2017 to December 2017. Patients presenting with lymphadenopathy were included in study after taking their informed consent. History regarding site of lymph node enlargement and residential address of patient (resident of area for past five years) was noted along with age and gender. Inadequate or insufficient tissue was excluded from study. All biopsies were received in formalin. Tissue was processed; slides were prepared and stained with Hematoxylin-Eosin stain. Slides were examined by two consultant pathologists and diagnosis was noted on the proforma. Patient's identity, age, gender, residence, site of lymph node biopsy, diagnosis was noted. All data was entered in SPSS 21 and descriptive statistics were used to obtain results of age, gender, site, residence and diagnosis. All variable were analyzed by descriptive statistics. Chi-Square test was used to see association between gender and diagnosis and frequency of various diagnoses among different areas of patient presentation.

Sampling Technique: Non-probability purposive sampling

Inclusion Criteria: All adequate lymph node biopsies were included.

Exclusion Criteria: Insufficient tissue or tissue that showed autolysis or crushing was excluded.

RESULTS

Our results showed that during year 2017, 308 cases of lymph node biopsy were received at pathology department, KEMU. Out of 308, 149 (48.4%) were males and 159 (51.6%) were females. Their ages ranged from 1 to 89 years and mean age was 25.1 ± 16.89 . Most common site of lymphadenopathy was cervical and then mesenteric both in males (31.8%, 8.4% respectively) and females (35.4%, 5.8%). After cervical and mesenteric, axillary (3.9%) and supraclavicular (1.6%) nodes were more commonly enlarged in females. Males presented more commonly with Inguinal (4.2%) and submandibular node (1.6%) enlargement when compared with females (Table I). Among male patients 108 (35.1%) were reactive, 1 (0.3%) showed abscess, 23 (7.5%) had TB, 4 (1.3%) showed ALP, 4 (1.3%) were of NHL, 2(0.6%) had HD, and 7 (2.3%) had metastatic carcinoma. In females 110

(35.7%) were reactive, 1(0.3%) had abscess, 33 (10.7%) had TB, 5 (1.6%) showed ALP, 2 (0.6%) had NHL, 1 (0.3%) had HD and 7 (2.3%) had metastatic disease. Regarding areas from where patients belonged 206 (66.9%) were from Lahore, 43(14%) from Sheikhupura, 19(6.2%) from Narowal, 17(5.5%) from Nankana, 11(3.6%) from Okara, 7(2.3%) from Mianwali, 5(1.6%) from Bahawalnagar. Most common site of lymphadenopathy was cervical lymph node enlargement 207 (67.2%), then mesenteric 44 (14.3%), inguinal 24 (7.8%), axillary 17 (5.5%), submandibular 9 (2.9%) and supraclavicular 7 (2.3%). The diagnosis of lymphadenopathy varied from reactive to malignancy as follows: 218 (70.8%) were reactive, 56 (18.2%) showed TB, 14 (4.5%) exhibited metastatic carcinoma, 9 (2.9%) were labeled as Atypical lymphoproliferative disorder, 6 (1.9%) were of Non-Hodgkin lymphoma, 3 (1.0%) of Hodgkin lymphoma and 2 (0.6%) of abscess. As we observed relationship of malignancy to site of lymph node enlargement, we concluded that out of 308 cases 276 (89.6%) were reactive, 9 (2.9%) remained undiagnosed as ALP and 23 (7.4%) showed malignancies. Most common site of metastatic malignancy presentation was cervical node (69.5%), then axillary (17.3%) then submandibular, inguinal and mesenteric (4.3% each). No malignancy was seen in supraclavicular lymph node. (Table II) Among the population of Lahore residents 146 (47.4%) were reactive, 40 (13 %) had tuberculosis, 9 (2.9%) had metastatic carcinoma, 5 (1.6%) were diagnosed as ALP, 3(1%) had NHL 2 (0.6%) had HD and only 1 (0.3%) had abscess. From Sheikhupura 26 (8.4%) patients had reactive nodes, 10 (3.2%) had tuberculosis, 2 (0.6%) had ALP, NHL and Metastasis each. Only 1(0.3%) case had abscess. Group from Narowal showed 12(3.9%) to be reactive, 3 (1%) each had TB and HD and 1 (0.3%) case of NHL.

Table No.I: Site of lymphadenopathy among males and females.

Site	Male	Female	Total
Cervical	98 (31.8%)	109(35.4%)	207(67.2%)
Subman-dibular	5(1.6%)	4(1.3%)	9(2.9%)
Supracla-vicular	2(0.6%)	5(1.6%)	7(2.3%)
Axillary	5(1.6%)	12(3.9%)	17(5.5%)
Inguinal	13(4.2%)	11(3.6%)	24(7.8%)
Mesenteric	26(8.4%)	18(5.8%)	44(14.3%)
Total	149(48.4%)	159(51.6%)	308(100%)

From Nankana out 17 cases 14 (4.5%) showed reactive nodes and 3(1%) had tuberculosis. Cases from Okara showed reactive hyperplasia in 9 (2.9%), 1 (0.3%) labeled as ALP and 1(0.3%) had HD. 7 (2.3%) cases belonged to Mianwali and all showed reactive hyperplasia. Cases that belonged to Bahawalnagar

showed reactive hyperplasia in 4 (1.3%) and 1(0.3%) was diagnosed as ALP. (Table 3) As we evaluated frequency of reactive hyperplasia, TB and malignancy in various age groups. We concluded that children

(under 18 years) and old patients (over 70 years) presented commonly with reactive nodes. Adults (19-69 y) showed more frequent involvement with tuberculosis and metastatic malignancy. (Table 4).

Table No.2: Frequency of causes of lymphadenopathy and their sites of presentation.

Site	Reactive	TB	ALP	NHL	HD	Abscess	Metastasis
Cervical	139 (45.1%)	44 (14.3%)	6 (1.9%)	5 (16%)	2 (0.6%)	2 (0.6%)	9 (2.9%)
Submandibular	7 (2.3%)	1 (0.3%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.3%)
Suprclavicular	7 (2.3%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Axillary	8 (2.6%)	3 (1.0%)	2 (0.6%)	0 (0%)	1 (0.3%)	0 (0%)	3 (1.0%)
Inguinal	19 (6.2%)	3 (1.0%)	1 (0.3%)	0 (0%)	0 (0%)	0 (0%)	1 (0.3%)
Mesenteric	38 (12.3%)	5 (1.6%)	0 (0%)	1 (0.3%)	0 (0%)	0 (0%)	0 (0%)
Total	218 (70.8%)	56 (18.2%)	9 (2.9%)	6 (1.9%)	3 (1.0%)	2 (0.6%)	14 (4.5%)

Table No.3: Frequencies of diagnoses from various residential areas.

Diagnosis	Lahore	Sheikhpura	Narowal	Nankana	Okara	Others	Total
Reactive	146(47.4%)	26(8.4%)	12(3.9%)	14(4.5%)	9(2.9%)	11(3.6%)	218(70.8%)
Abscess	1(0.3%)	1(0.3%)	0(0%)	0(0%)	0(0%)	0(0%)	2(0.6%)
TB	40(13%)	10(3.2%)	3(1%)	3(1%)	0(0%)	0(0%)	56(18.2%)
ALP	5(1.6%)	2(0.6%)	0(0%)	0(0%)	1(0.3%)	1(0.3%)	9(2.9%)
NHL	3(1%)	2(0.6%)	1(0.3%)	0(0%)	0(0%)	0(0%)	6(1.9%)
HD	2(0.6%)	0(0%)	0(0%)	0(0%)	1(0%)	0(0%)	3(1%)
METS	9(2.9%)	2(0.6%)	3(1%)	0(0%)	0(0%)	0(0%)	14(4.5%)
Total	206(66.9%)	43(14.0%)	19(6.2%)	17(5.5%)	11(3.6%)	12(3.9%)	308(100%)

Table No.4: Frequency of diagnosis according to age groups.

Diagnosis		Age groups			Total
		Under 18	19-69	70 and above	
	Reactive	112(36.4%)	101(32.8%)	5(1.6%)	218(70.8%)
	Abscess	1(0.3%)	1(0.3%)	0	2(0.6%)
	TB	20(6.5%)	36(11.7%)	0	56(18.2%)
	ALP	4(1.3%)	5(1.6%)	0	9(2.9%)
	NHL	2(0.6%)	4(1.3%)	0	6(1.9%)
	HL	2(0.6%)	1(0.3%)	0	3(1.0%)
	Metastatic CA	0(0%)	14(4.5%)	0	14(4.5%)
Total		141(45.8%)	162(52.6%)	5(1.6%)	308(100%)

DISCUSSION

In our study, age range of lymphadenopathy of 308 cases was 1-89 years with mean of 25.1±16.89. Similar study conducted on 185 patients in Turkey showed an average age of 41.01 ± 20.62 years¹⁰. This is much higher than our age range. However age range matched with ours and was 1-86 years. Their patient population comprised of 47% females and 53% males. Our group had 51.6% females and 48.4% males. So in our group females predominated.

Most common site of lymph node enlargement was cervical node and was reactive (45.1%). This is in accordance with findings of Mohseni S, who also found this enlargement was frequently due to reactive changes¹¹. Iqbal et al showed that 70.45% of cervical lymphadenopathy was due to TB and only 13.63% was

due to reactive changes¹². Upadhyay N reported a rare case of cervical lymphadenopathy as only presentation of NHL¹³. Therefore cervical lymph node should be screened with caution as it can be either benign or malignant. Tracy JC observed metastatic malignancy in all supraclavicular nodes¹⁴. This is in contrast with our findings as we did not observe metastasis in supraclavicular nodes, rather they were all reactive. (Table 2) We found out that metastasis was most common in cervical (2.9%) and then axillary nodes (1.0%).

Sibanda EN reviewed all lymph node biopsy reports collected at Histopathology unit in Harare, Zimbabwe. The commonest diseases in 2194 lymph node specimens submitted were: (a) non specific hyperplasia (33%); (b) tuberculous lymphadenitis (26.7%); (c) metastases (12.4%); (d) Kaposi's sarcoma (9%); (e)

lymphomas (7%).⁴ In our study out of total 308 cases, 218 (70.8%) were reactive, 56 (18.2%) showed TB, 14 (4.5%) exhibited metastatic carcinoma, 9 (2.9%) were labeled as Atypical lymphoproliferative disorder, 6 (1.9%) were of Non-Hodgkin lymphoma, 3 (1.0%) of Hodgkin lymphoma and 2 (0.6%) of abscess. Similarly Vali et al reported reactive nodes in 54.2% of patients and malignant in 11.4% of patient population.¹⁵

Saini stated that infection was predominantly diagnosed in younger patients, sarcoidosis in the middle aged, and tumor in older patients ($p < 0.001$).¹⁶ We concluded that young and old patients had reactive nodes while malignancy was seen in middle age group. (Table 3)

Toraks reviewed data of 69 tuberculous patients in Rabat in 2016. He observed female (70%) and a young age predominance of patients (31.4 year $\pm$ 13.1).¹⁷ We also observed female predominance (10.7%) in tuberculous infection as compared to males (7.5%). As Qadeer E et al reported increasing prevalence of tuberculosis with age and 1.8 times higher among older men than women. Their data also suggested under-detection and/or -notification of TB, especially among young men and elderly.⁸ Many studies like Begum A, Fazal et al reported tuberculosis in females and commonly in cervical nodes.^{18,19} In children, abdominal tuberculosis is more prevalent.²⁰ In contrast to that our patients under 18 showed reactive hyperplasia to be commoner than tuberculosis. (Table 4)

According to AA armadas, the prevalence of malignancy in a primary care set up, associated with unexplained lymphadenopathy was as low as 1.1%. However, in referral centers, the prevalence of malignancy was found to be 40%–60%. NHL is considered as the fourth common worldwide malignancy in males with a frequency of 6.1%.²¹ Our results showed frequency of NHL to be 1.9% and HD was 1.0%. NHL was common in both males (1.3%) and females when compared with HD (0.6%, 0.3%).

As we analyzed areas from where patients belonged, we concluded that 66.9% of patients were from Lahore. Most common cause of lymphadenopathy was reactive hyperplasia and tuberculosis was second most common cause. Similar findings were seen in Sheikhpura, Nankana and Narowal patients. Patients who belonged to Okara, Mianwali and Bahwalnagr showed reactive hyperplasia and malignancy. Tuberculosis was not seen in them. Reactive Hyperplasia can be diagnosed with the help of simple test like Fine needle aspiration. For this ailment patients had to travel a long way to Lahore to get diagnosed. If this simple test is available there, expense of travel and stay can be avoided which will help patient population. We could not find any local study to compare with these findings.

CONCLUSION

Reactive lymph node enlargement is most common cause of lymphadenopathy in tertiary care setup.

Tuberculosis is second most common cause, seen more in females. Mayo Hospital is catering a large number of patients from cities other than Lahore. It is suggested that tertiary care services should be strengthened in areas surrounding Lahore to lower patient burden and improve health facilities at Mayo Hospital. Government hospitals should be equipped with special tests like immune-markers and molecular techniques to precisely diagnose lymphoid malignancies.

Author's Contribution:

Concept & Design of Study:	Samina Qamar
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Data Analysis:	Ahmad Hameed, Sobia Ashraf
Revisiting Critically:	Samina Qamar, Shahid Mahmood
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Conflict of Interest: The study has no conflict of interest to declare by any author.

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Frequency of Iron Deficiency Anemia in Chronic Kidney Disease Patients on Hemodialysis

Hemodialysis in
Kidney Disease
due to Iron
Deficiency
Anemia

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Muhammad Bilal Khattak⁴

ABSTRACT

Objective: To determine the frequency of iron deficiency anemia among chronic kidney disease patients on hemodialysis therapy.

Study Design: Descriptive / cross sectional study

Place and Duration of Study: This study was conducted at the Nephrology Unit, Institute of Kidney Diseases Hayatabad Peshawar from November 2016 to November 2017.

Materials and Methods: The study was conducted at Nephrology Dialysis unit of institute of Kidney Diseases (IKD) Hayatabad Medical Complex Peshawar Pakistan. Hospital based descriptive cross-sectional study. The study duration was one year. Total sample size was 204 using 15.4% prevalence of IDA in CKD, 95% confidence level 5% margin of error with the help of WHO software for sample size determination.

Results: The study was conducted on 204 patients presented with CKD for dialysis. The mean age of our sample was 38.81 years with a standard deviation of 15.202. We divided the patients in 3 different age groups. Patients in age groups from 18-33 years were 42.2% of patients, in the age group 34-48 years we had 21.6% patients and in age group ≤ 60 years we had 36.3% of patients. Iron deficiency anemia was observed in 126 (61.8) patients while 78 (38.2) patients have no iron deficiency anemia.

Conclusion: Anemia is a common complication among patients with chronic kidney disease. Early detection and treatment of anemia would definitely improve quality of life and reduce the burden of care.

Key Words: Chronic Kidney Disease, Anemia, GFR

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INTRODUCTION

Chronic kidney disease (CKD) is defined as a damage to the kidneys affecting its structure and function with glomerular filtration rate (GFR) of less than 60 mL/min/1.73 m² for three month and or more three months, irrespective of clinical identification of the disease^{1,2}. There is certain limit to the condition when the nephrons damage exceeds that limit and the functional impairment of the kidneys reaches and overshoot that limit a status is characterized with Whatever the underlying etiology, once the loss of nephrons and reduction of functional renal mass reaches a certain point, the remaining nephrons begin a

process of irreversible sclerosis that leads to a progressive decline in the GFR. CKD can have a variety of different presentations depending on the stage of the disease and its cause, as well as patient factors such as age. CKD is common condition that is more prevalent in the elderly population. One of the most common complications of the chronic kidney disease is iron deficiency anemia. Anemia is defined as a level of $< 13\text{g/dL}$ in men and $< 12\text{g/dL}$ in women respectively.³ IDA is one of the most common causes of anemia in developing countries of the world. The basic pathology and reason for causation of anemia in patients with CKD are multiple. Out of all these reasons erythropoietin deficiency is the most important one. Other causes and factors responsible are decreased red blood cell survival in CKD, nutritional deficiency, endocrine involvement and bleeding diathesis^{4,5}. The term CKD is used for group of disorders which affect structure and or function of the kidneys. There is an extensive variation in the disease and is dependent on etiology, pathology and progression of the disorder. The disorder is not only an area of interest and worry for nephrologists but also for medical specialists and general physicians after guidelines have recommended kidney disease as a life-threatening disorder affecting population and needs care by not only nephrologists but also general practitioners and internists⁵.

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According to the guidelines the disorder has become a public health problem to help people in its prevention, early detection and management. The purpose of this study was to determine the frequency of iron deficiency anemia in patient with chronic kidney disease (CKD) on hemodialysis. National Kidney foundation's kidney Dialysis out comes quality initiative (K/DOQI) guideline defines CKD as kidney damage or estimated glomerular filtration rate (eGFR) of $< 60\text{ml/min } 1.73\text{m}^2$ for ≥ 3 months. Grading of CKD is achieved by calculating either the creatinine clearance using the modified Cockcroft-Gault equation or the estimated glomerular filtration rate (eGFR) by use of the Modification of Diet in the Renal Diseases (MDRD) equation. NKF-K/DOQI guidelines define CKD as follows⁶.

Stage	Description	GFR(ml/min 1.73m^2)
1	Kidney Damage with normal or Elevated GFR	≥ 90
2	Kidney Damage with mild or Decreased GFR	60-89
3	Moderate decrease GFR	30-59
4	Severe decrease	15-29
5	Kidney failure	<15 (or dialysis)

The guidelines also classified CKD based on severity and therapeutic intervention required of each stage for slowing progression of the disease and treatment of complication, such as anemia and metabolic abnormalities. Stage 4 is severe impairment with severe decreased e GFR $15-29\text{ ml/min per } 1.73\text{m}^2$ in which the focus of care is appropriate preparation for renal replacement therapy and stage 5 defined as established renal failure with e GFR <15 which is accomplished in most cases by sign and symptoms of uremia, such patients require renal replacement therapy (dialysis and renal transplantation)⁶. Both incidence and prevalence in patients with CKD has increased globally in both developed and developing countries⁷.

Iron deficiency has been considered as important cause of anemia in CKD patients and these patients manifest iron deficiency as "absolute "or functional" iron deficiency. In CKD patients iron stores are low or even absent as a result of poor intake of nutrition mainly associated with poor appetite resulted by uremia and increased loss through chronic GIT bleeding due to blood vessel fragility associated with uremia, platelet dysfunctional related to uremia, chronic blood retention in the dialysis circuit⁸. Functional iron deficiency appears when the body needs bigger quantity of iron for restoration of normal hemoglobin blood level and it is not supported by its nominal release from iron store in CKD patient's macrophages and hepatocytes to transferring⁸. In India, Talwar et al studied hematological profile in 27 chronic renal failure patients and the prevalence of anemia was 94% of

which 60% had microcytic hypochromic anemia with serum ferritin low in 62%, serum iron below in 74% of the patients and bone marrow iron study revealed 57% of cases had negative bone marrow iron store⁹. Several conducted on Chronic Kidney Disease patients concluded iron deficiency anemia as common problem in these patients^{9,10,11}.

MATERIALS AND METHODS

The study was conducted at Nephrology Dialysis unit of institute of Kidney Diseases (IKD) Hayatabad Medical Complex Peshawar Pakistan. Hospital based descriptive cross-sectional study. One year. Total sample size was 204 using 15.4% prevalence of IDA in CKD, 95% confidence level 5% margin of error with the help of WHO software for sample size determination. All hemodialysis dependent patients being dialyzed at IKD Hayatabad Peshawar with dialysis depending defined as being maintained on regular hemodialysis for the past 3 months and with age limit of 18-60 years was included in the study. Pregnant women patient under 18 years of age and not on hemodialysis. This study was conducted after approval from Hospital ethical and research committee. All out door patients meeting the inclusion criteria were included in the study. The purpose and benefits of study were explained to the patient and a written informed consent were obtained. All patients were subjected to detailed history and examination. They were assured of confidentiality of all data. All the information including name, age, gender and address were recorded in the study proforma. Strict exclusive criteria were followed to control confounders and bias in study result. 5ml of pre dialysis blood was collected in a BD disposable syringe. It was transferred to EDTA and serum vacutainer for estimation of hemoglobin level and ferritin level. Hemoglobin (Hb) estimation was performed on automated hematology analyzer Model sysmex kx-21 and serum ferritin assay was done on (cobas e411 immunoassay analyzer) Roche ECL technology at main Laboratory of IKD.

Data collected was entered in SPSS (Statistical Package for social sciences) version 17. Mean $\pm$ Sd were calculated for quantitative variables like age, Hb and serum ferritin level. Frequency and percentage were calculated for categorical variables like gender and iron supplement to see effect modifiers. Results were presented as tables and graph/charts.

RESULTS

The study was conducted on 204 patients presented with CKD for dialysis at nephrology unit IKD HMC Peshawar from November 2016 to November 2017. The mean age of our sample was 38.81 years with a standard deviation of 15.202. We divided the patients in 3 different age groups.

In age groups from 18-33 years we had 42.2% of patients, in the age group 34-48 years we had 21.6% patients and in age group ≤ 60 years we had 36.3% of patients as given table 1.

Out of 204 patients included in the study there were 119 (58.33%) male patients and 85 (41.67) female patients. The mean and standard deviation of hemoglobin was 9.01 ± 1.93 and number of hemodialysis was 1.92 ± 0.453 in patient having IDA in CKD. The mean number of blood transfusion was observed as 1.30 ± 1.39 .

Out of 204 patients 160 (78.4%) patients had used iron supplementation while 44 (21.6%) patients have not used iron supplementation. (Table 2)

Table No. 1: Age group wise distribution of Sample (n=204)

Age Groups (years)	Frequency	Percent
18-33	86	42.2
34-48	44	21.6
≤ 60	74	36.3
Total	204	100.0

Table No. 2: Frequency of patients taking iron supplementation

Iron Supplementation	Frequency	Percent
Yes	160	78.4
No	44	21.6
Total	204	100.0

Table No. 3: Frequency of Iron deficiency Anemia in sample (n=204)

Iron deficiency anemia	Frequency	Percent
Yes	126	61.8
No	78	38.2
Total	204	100.0

Table No. 4: Age group wise stratification of Iron Deficiency Anemia (n=204)

Age Groups	Iron Deficiency Anemia		Total	p-value
	Yes	No		
18-33	57	29	86	0.42
	66.3%	33.7%	100.0%	
34-48	20	24	44	
	45.5%	54.5%	100.0%	
≤ 60	49	25	74	
	66.2%	33.8%	100.0%	
Total	126	78	204	

Out of 204 patients iron deficiency anemia was observed in 126 (61.8) patients while 78 (38.2) patients have no iron deficiency anemia (Table 3)

We stratified iron deficiency anemia with regards to different age groups and observed that the difference was statistically significant with a P value of 0.42 (Table 4) we stratified the iron deficiency with regards to gender and observed that the difference was statistically insignificant with a P value of 0.884 (Table 5) we stratified the iron deficiency with regards to iron supplement and observed that the difference was statistically insignificant with a P value of 0.323 (Table 6).

Table No. 5: Iron Deficiency Anemia stratification related to gender

Gender	Iron Deficiency Anemia		Total	p-value
	Yes	No		
Male	74	45	119	0.884
	62.2%	37.8%	100.0%	
Female	52	33	85	
	61.2%	38.8%	100.0%	
Total	126	78	204	
	61.8%	38.2%	100.0%	

Table No. 6: Cross tabulation of Iron deficiency anemia and Iron supplementation

Iron Supplementation	Iron Deficiency Anemia		Total	p-value
	Yes	No		
Yes	96	64	160	0.323
	60.0%	40.0%	100.0%	
No	30	14	44	
	68.2%	31.8%	100.0%	
Total	126	78	204	
	61.8%	38.2%	100.0%	

DISCUSSION

Anemia is a common complication among patients with CKD. Early detection and treatment of anemia would definitely improve quality of life and reduce the burden of care.

This study recruited CKD patients among patients with different kidney diseases seen at IKD HMC Peshawar. The nephrology unit at IKD is the first and the only unit in a public hospital offering care and treatment for kidney diseases patients. The unit serves patients for the whole province, thus the study is a tertiary care hospital based.

The majority of study subjects were Male (58.33%) in line with several other studies emulating the fact^{12,13} as men suffer CKD more than females due to fact that in developing countries men tend to seek medical attention more than females.

The mean age in this study was 38.81 ± 15.202 years which was similar finding and 45.0 ± 15.0 and 47.0 ± 2.0 years in the Nigerian and Indonesia study respectively.¹⁴⁻¹⁵

Thus average age in this study is on the other hand is another reminder that increasing age is a traditional risk factor for CKD as age increases eGFR decreases, therefore, CKD is common in adult as compared to young age Hypertension and diabetes mellitus were identified as main underlying diseases for CKD in this study.

In this study (61.8%) of CKD patients were iron deficient as indicated by serum ferritin $<100\text{ng/ml}$ and hemoglobin level was 9.01 ± 1.93 which is in agreement with another study done by HSU et al reported 62.6% of CKD patients with anemia are iron deficient as indicated by serum ferritin $<100\text{ng/ml}$.

CONCLUSION

Anemia is a common complication among patients with chronic kidney disease. Early detection and treatment of anemia would definitely improve quality of life and reduce the burden of care.

Author's Contribution:

Concept & Design of Study:	Malik Zeb
Drafting:	Shahtaj Khan
Data Analysis:	Muhammad Aqeel Khan, Muhammad Bilal Khattak ⁴
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Final Approval of version:	Malik Zeb, Shahtaj Khan

Conflict of Interest: The study has no conflict of interest to declare by any author.

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Frequency of Thrombotic Microangiopathy in Patients with Pregnancy Related Acute Kidney Injury

Thrombotic
Microangiopathy
with Pregnancy
Related Acute
Kidney Injury

Fazal Mohammad¹, Fozia Mohammad Bakhsh² and Syed Mohkam¹

ABSTRACT

Objective: To determine the Frequency of thrombotic micro-angiopathy in patients with pregnancy related acute kidney injury.

Study Design: Cross-sectional study.

Place and Duration of study: This study was conducted out at Department of Nephrology, Baluchistan Institute of Nephro-Urology, and Department of Obs and Gynae, BMCH Quetta from July 2016 to December 2017.

Material and Methods: A heterogeneous disease called Pregnancy-related acute kidney injury (P-AKI) that occurs due to a large number of important etiologies. Although a rare but a fatal cause of P-AKI is pregnancy associated Thrombotic microangiopathy (TMA), with very poor consequence. Patient survival pregnancy and kidney outcome is dependent on early diagnosis and prompt treatment. The two most common disorder of thrombotic microangiopathies (TMA) are TTP (thrombotic thrombocytopenic purpura) and HUS (hemolytic uremic syndrome). In this study we would determine the frequency of thrombotic microangiopathy in patient with pregnancy related acute kidney injury. Among the patients admitted in department of gynecology and obstetrics during this period, who developed AKI, MAHA and unexplained thrombocytopenia were enrolled. Modified Jaffe's technique was used to measure serum creatinine whereas Modification of Diet in Renal Disease (MDRD) equation was used to measure glomerular filtration rate. Acute Kidney Injury was defined as when the urine output decreased to less than 400 mL for more than 6 h or serum creatinine increased about 1.5 times from the baseline or both. Thrombotic microangiopathy was further classified into TTP and a HUS. ADAMS-TS-13 levels were sent. Data was collected on predesigned Performa. Non-probability consecutive sampling technique was used for sample collection. After accomplishment of data of required sample, a statistics was established on SPSS version 22.0 for data analysis. For continuous variables such as age the mean, median and standard deviation was calculated. For qualitative variables Pearson Chi-square test (χ^2) was applied whereas t-test was applied for all continuous variables. P-value < 0.05 considered as significant.

Results: 2763 patients were admitted in department of Gynecology, 221 patients (8%) were diagnosed as pregnancy related AKI (P-AKI). among them 26 patients (11%) had pregnancy related thrombotic microangiopathy (P-TMA) as a cause of AKI. 19 patients were having TTP and 7 had HUS. 15 Patients were nulliparous while 11 were multiparous. The mean age was 29.5 ± 3.8 years. Most of TTP patients 15/19 presented antepartum while 4/19 postpartum. HUS developed in all patients in postpartum period. 50 % of the patients with TTP required dialysis initially but only 10 % developed ESRD. In HUS group 90 % required dialysis initially and 80 % remained dialysis dependent. thrombocytopenia was more severe in TTP group while renal failure in HUS.

Conclusion: The spectrum of thrombotic microangiopathies (TMA) during pregnancy has very complex presentation. Although very difficult to differentiate from acute fatty liver of pregnancy and HELLP syndrome yet is very necessary as each of them have entirely different management. Early identification and prompt treatment with plasmapheresis, plasma exchange, pulsed steroid therapy and if required dialysis can decrease the maternal and neonatal mortality risk and improve the outcome of both.

Key Words: Pregnancy, pregnancy related acute renal injury, pregnancy related Thrombotic microangiopathy, TTP, HUS

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INTRODUCTION

Pregnancy related acute kidney injury (P-AKI) is considered as an entity of heterogeneous disease that

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happens due to a large number of underlying etiologies¹. A very uncommon and lethal medical condition known as Thrombotic Microangiopathy (often known simply as TMA)². Which damages the body's vital organs like kidney and brain by involving their smallest blood vessels³.

TMA in pregnancy is important although rare cause of P-AKI. The patient may present during pregnancy or postpartum with low platelets (<150) usually less than 50K, hemolysis as evident by MAHA, raised LDH and indirect bilirubin. Sometimes neurological symptoms like fits, decreased conscious level may also be seen. TTP usually present in second or third trimester and HUS usually in postpartum period⁴.

Normal pregnancy is a procoagulant state. in order to protect hemorrhage at the time of labor few haemostatic changes occur, which are hormonally mediated.

TTP is caused by deficiency of ADAMTS 13 (a disintegrin and metalloprotease with thrombospondin type 1 motif, member 13) (5). ADAMTS 13 is mandatory to cleave von Willebrand factor (VWF). Lack of ADAMTS13 either acquired or inherited (IgG autoantibodies to ADAMTS13) results in accumulation of ultra large VWF multimers leading to platelet aggregation and thrombosis in micro vessels. Von Willebrand Factor (VWF) levels increase during pregnancy, returning back to normal 6 weeks postpartum. VWF and ADAMTS13 have a reciprocal relationship. In second and third trimesters of normal pregnancy, ADAMTS13 activity decreases both because of excess substrate (vWF) and effect of estrogen, while VWF levels increase⁶. This is the reason that TTP is seen more commonly in pregnancy⁷.

In HUS mutation occurs in complement genes of the alternative complement pathway, such as CD46 (also termed MCP), CFH (Factor H), CFI (Factor I)⁷, Factor B or C3, complement-activating genes⁸.

Approximately 15–30% of all cases of a HUS is due to CFH mutations⁽⁸⁾. 10-13% of CD46 mutations occurs in a HUS patients, the mostly being heterozygous and these patients have a milder clinical sequence⁹.

In medical practice it becomes sometimes hard to distinguish clinically among TTP, HUS, PE, and HELLP but yet is very important as the management is entirely different.

Severe thrombocytopenia very high LDH, second or third trimester presentation, prominent neurological symptoms, less severe renal failure, failure of resolution of thrombocytopenia and high LDH three days after delivery, ADAMTS 13 levels <10% all suggest TTP.

In contrary more severe renal failure, postpartum presentation, ADAMTS 13 level >10%, mutations of factors involved in alternate complement pathway, persistence of hematological abnormalities and renal dysfunction after delivery, failure of resolution of renal failure with plasmapheresis, rapidly progressive postpartum acute kidney injury without an apparent cause for acute tubular necrosis, all suggest HUS.

In this study we would determine the frequency of thrombotic microangiopathy in patient with pregnancy related acute kidney injury.

MATERIALS AND METHODS

Cross-sectional study was conducted in Department of Nephrology, Baluchistan Institute of Nephro-Urology, Quetta, and Department of Obstetrics and Gynecology BMCH in a period of 18 months from month of July 2016 to December 2017. Ethical committee approval was obtained before conducting the study. Among 2763 patients admitted in department of gynecology and obstetrics during this period, 26 patients were enrolled.

The inclusion criteria comprise all patients with evidence of AKI, MAHA, thrombocytopenia, raised LDH, normal coagulation profile, neurological abnormalities without another apparent cause like HELLP, AFLP, PE. TMA was categorized as TTP and HUS. ADAMTS 13 levels were sent. Patients with MAHA, more severe thrombocytopenia and neurological involvement, ADAMTS 13 levels <10% were categorized as TTP, while patients with more severe renal failure, less severe thrombocytopenia and neurological involvement and ADAMTS 13 level >10% were labelled as HUS¹⁰.

For Data collection predesigned Proforma was used. In which patient's medical registration no, age, complete history, physical examination and laboratory tests were included. Informed consent was obtained from all participants. The non-probability consecutive sampling was used for sampling technique. After accomplishment of data of required sample, a statistics was established on SPSS version 22.0 for data analysis. For continuous variables such as age the mean, median and standard deviation was calculated. For qualitative variables Pearson Chi-square test (χ^2) was applied whereas t-test was applied for all continuous variables. P-value < 0.05 considered as significant.

RESULTS

Of 2763 admitted patients in department of Gynecology, 221 patients (8%) were diagnosed as pregnancy related AKI (P-AKI). Among them 26 patients (11%) had pregnancy related thrombotic microangiopathy (P-TMA) as a cause of AKI. The mean age of patients is 29.5±3.8 years. Of those 26 females, 15 were nulliparous and 11 were multiparous. With respect to thrombotic microangiopathies, 19 patients were found TTP, and 7 were diagnosed as aHUS which constitute of 73.1% and 26.9% respectively (Table 1).

Table No. 1: Thrombotic Microangiopathies

Thrombotic Microangiopathies	19	73.1 %
• TTP	7	26.9 %
• HUS		

Table No.2: Frequency and their percentage

	Frequency	Percentage
Parity		
Nulliparous	15	60%
Multiparous	11	40 %

Concerning parity, out of 7 nulliparous, 5 of them had TTP and remaining 2 had HUS. On the other hand, of total 19 multiparous, 14 were found to have TTP and remaining 5 were diagnosed as a HUS.

15/19 (80%) of the patients presented with TTP presented in second or third trimester and only 4/19 (20 %) postpartum, while all HUS 7/7 (100%) patients present after delivery.

TableNo. 3: Time of presentation

TMA (26)	Time of presentation	
	2 nd or 3 rd time	Post-partum
TTP(19)	80% (15/19)	20%(4/19)
HUS(7)	0% (0/7)	100% (7/7)

All patients in our study developed AKI, less severe in TTP group, more severe in HUS arm. in patients with TTP 9/19 patients(50 %)required dialysis,17/19 (90%)gained their renal functions back within 3 weeks but 2/19 patients(10 %) remained dialysis dependent. While in HUS 6/7 patients (90%) patients required dialysis and 5/7 patients (80%) got ESRD.

Table No. 4: Out Come

TMA (26)	Out Come	
	Initial requirement of dialysis	Dialysis dependent
TTP (19)	50 % (9/19)	10 % (2/19)
HUS (7)	90 % (6/7)	80% (5/7)

Table No.5: Laboratory investigations in patients with pregnancy related acute kidney injury

	Microan-giopathies	N	Mean $\pm$ Std. Deviation	P-value
TLC	TTP	19	12.52 $\pm$ 5.13	0.93
	aHUS	7	12.71 $\pm$ 4.71	
Hb	TTP	19	11.26 $\pm$ 1.62	0.56
	aHUS	7	10.85 $\pm$ 1.34	
Platelets	TTP	19	75.71 $\pm$ 8.38	0.03*
	aHUS	7	84.68 $\pm$ 6.60	
PT	TTP	19	13.47 $\pm$ 1.95	0.81
	aHUS	7	13.28 $\pm$ 1.38	
APTT	TTP	19	33.78 $\pm$ 3.58	0.89
	aHUS	7	34.00 $\pm$ 4.04	
AST	TTP	19	136.47 $\pm$ 6.72	0.62
	aHUS	7	126.28 $\pm$ 43.70	
ALT	TTP	19	137.68 $\pm$ 49.04	0.92
	aHUS	7	135.57 $\pm$ 48.33	
Total Bilirubin	TTP	19	6.53 $\pm$ 4.24	0.46
	aHUS	7	5.18 $\pm$ 3.47	
Direct bilirubin	TTP	19	3.87 $\pm$ 2.34	0.18
	aHUS	7	5.37 $\pm$ 2.83	
Indirect bilirubin	TTP	19	2.93 $\pm$ 1.12	0.89
	aHUS	7	3.00 $\pm$.93	
serum creatinine	TTP	19	2.40 $\pm$ 1.35	0.04*
	aHUS	7	4.30 $\pm$ 2.43	
SBP	TTP	19	125.73 $\pm$ 26.14	0.83
	aHUS	7	123.57 $\pm$ 9.16	
DBP	TTP	19	82.73 $\pm$ 11.11	0.80
	aHUS	7	83.85 $\pm$ 4.98	

DISCUSSION

The study determines the frequency of thrombotic microangiopathy in patients with pregnancy. Pregnancy related acute kidney injury is a life-threatening condition.TMA is one of the important cause of pregnancy related acute kidney injury.TMA is defined as the presence of fibrin and/or platelets thrombi in the arterioles and capillaries of vital organs, mostly affecting the brain and kidney histologically. TMA presents with swelling of endothelial cells, sub endothelial accumulation of protein and cell debris, and in certain cases, splitting of the glomerular basement membrane⁴.

TMA presenting with predominantly renal failure is usually called hemolytic uremic syndrome (HUS), while more severe thrombocytopenia with neurological involvement is defined as thrombotic thrombocytopenicpurpura (TTP), but overlap may occur: 10% cases of TTP patients have AKI, and neurologic involvement is not uncommon in typical HUS or aHUS¹¹.

TMA in pregnancy still has increase morbidity and mortality (up to 10%) rates¹². ADAMTS13 deficiency-related TMA (TTP) happens mostly during the second and third trimesters of pregnancy. In our study, most patients with TTP15/19(80%) presented in either second or third trimester of pregnancy while 4/19 (20%) presented postpartum. this finding in our study is consistent with the literature review, where pregnancy triggered TTP in 23 cases in which 83% of cases were seen in second or third trimesters¹³. These finding may be due to progressive decrease in ADAMTS13 and the similar increase in vWF antigen during normal pregnancy¹².

HUS mainly presents in post-partum period ,our patients with HUS 7/7 (100%) developed it postpartum, but it may be develop prepartum during second or third trimester as observed by Bruel et al (14),where 24% patients developed HUS before delivery and 76% patients presented postpartum . Dysregulation of the alternative complement pathway during postpartum period is caused bygene mutation encoding complement proteins. Numerous factors which leads to trigger the complement activation in an already genetically susceptible individual such as, preeclampsia, drugs, cancer, maternal–fetal hemorrhage, inflammation and infections. Most of our patients with TTP (14/19) and HUS (5/7) had TMA presentation in either first or second pregnancy while TMA developed in few multiparous women. This finding is consistent with retrospective study from the Spanish registry¹⁵ where they found that 73% patients had TMA presentation in first pregnancy.

While Fadifa khouri et al¹⁶ found that most patients presented in second pregnancy. The exact etiology that patients are more prone in first and second pregnancies is not known.

TTP presents with less severe renal failure and rarely becomes dialysis dependent. In our study 100% patients had renal failure with mean serum creatinine (2.40 mg/dl), but only 50% required dialysis and only 10% (2 patients) landed up on permanent hemodialysis. HUS has a very dismal renal outcome. Most of the patients develop CKD and become dialysis dependent. In our study among 7 patients with HUS, 6 (90%) required dialysis initially but 5/7 patients (80%) developed ESRD and were dependent on dialysis by the end of three months. It may be because of the reason that none could receive Eculizumab although all patients were plasmapheresis. In contrast to Huerta et al¹⁵ who reported that 33% patients who could not receive eculizumab developed ESRD, our 80% patients got ESRD. However, French group has reported a high incidence of ESRD i.e. 62% during the first month and 76% requiring RRT at the end of the follow-up¹⁷. Treatment modality also has significant impact on thrombotic microangiopathies. Plasmapheresis should be started immediately after suspecting TMA, not waiting for ADAMTS 13 levels. Early plasmapheresis improves outcome both hematological and renal in TTP while only hematological in HUS. Pulse steroid therapy may be given as an adjunct therapy with plasmapheresis in TTP, platelet transfusions should be avoided, but only in case of bleeding, blood transfusion when required. In case of postnatal TMA, eculizumab must be given as early as possible to improve renal recovery¹⁶. The eculizumab regimen includes four weekly 900-mg infusions followed by 1,200-mg infusions every fortnight. We could not use Eculizumab as treatment option in HUS as this medicine is not available in this part of the world, and our patients could not afford either.

CONCLUSION

Conclusion: The spectrum of thrombotic microangiopathies (TMA) during pregnancy has very complex presentation and therefore very difficult to differentiate. Early identification and prompt treatment with plasma exchange, plasmapheresis and pulsed steroid therapy, Eculizumab can lessen the risk of neonatal and maternal mortality and improve the outcome of both of them.

Recommendation: The study highlights the spectrum of TMA in pregnancy related acute renal injury and its outcome. Therefore, we recommend that institutions, especially in Pakistan, should adopt a policy for early identification and quick treatment of TMA in pregnancy in order to decrease the risk of both mother and infant mortality and morbidity.

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Author's Contribution:

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Conflict of Interest: The study has no conflict of interest to declare by any author.

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Toxic Effect of Isoniazid Hydrochloride on Liver and Reversal of it by Curcuma Longa

Isoniazid
Hydrochloride &
Reversal by
Curcuma Longa

Mujahid Akbar Mamoun¹, Jawad Mumtaz Sodhar², Sama-ul-Haq³ and Mazhar ul Haque¹

ABSTRACT

Objective: Isoniazid Hydrochloride is a drug used for prophylaxis and treatment of tuberculosis with the combination of other drugs.

Study Design: Experimental study.

Place and Duration of Study: This study was conducted at the at Shahida Islam Medical College, Lodhran, during July 2017 to December 2017.

Materials and Methods: The present study was conducted on 30 rabbits which were group from A to C consisting of 10 rabbits in each group with the weight of 2500-3500 grams. The first control group A was fed on fresh alfalfa and water, the second group B was given 50 mg per kilogram body-weight of INH dissolved in water twice a day and the third group C was given INH with curcuma longa 100 mg twice a day dissolved in water in powder form. The blood samples were taken on day 01, 10 and 20.

Results: The AST level has non-significant changes in group A where P value was 0.21. The changes in group B and C are significant where P value in both were 0.01. In group B the AST level raised high during initial ten days where as AST level came down on day 20 probably due to addition of curcuma longa. The level of AST has remained close to normal in group C due to addition of high dose of curcuma longa. The liver parenchymal damage was observed on treatment with INH in group B. The restoration of hepatocytes architecture and minimum fibrosis was observed in group C.

Conclusion: Curcuma longa has protective effect against all the toxic agents of the liver. Curcumin has several group which function as antioxidant²⁰. It has been proved practically that curcuma longa is very effective against the Hepatotoxic agents.

Key Words: Curcuma longa, hepatotoxic, Isoniazid hydrochlorid.

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INTRODUCTION

Since 1952, isoniazid is used for the treatment of tuberculosis¹. It does not allow the the cell membrane of the bacteria to be formed. So, the proliferation of the Mycobacterium Tuberculae is stopped. Isoniazid is not only used for the treatment of tuberculosis but also used for its prophylaxis². The membrane of the mitochondria has the same configuration, as the cell membrane has, so the wall of the mitochondria is disrupted, damaging the hepatocytes and produced the hepatotoxicity³, 10-20%

of the people on INH can raise their ALT, in the beginning of the use of the drug. Neither only ALT but also AST also raised in first two months of the start of the drug. After 3-6 months, the enzymes become normal if the use of the drug is stopped⁴. Many infections can cause damage in the form of viruses, bacteria and helminthiasis. Multiple other factors are available, can cause damage to liver, such as antibiotics, anticonvulsants, psychotropic drugs and abuse of alcohol⁵. Non alcoholic fatty liver disease (NAFLD) is also a big cause of chronic liver failure⁶. Liver can be injured at the level of hepatocytes, Kupffer cells, bile canaliculi and sinusoidal epithelial cells. All these injuries bringing the result as liver dysfunction⁷. These liver injuries are more common in old people and females than young people and males respectively⁸. There are different species of Curcuma Longa. Curcuma is the commonest one used in daily diet. The most active ingredient present in curcuma longa is Curcumin⁹. Turmeric or curcuma longa is a herbaceous plant which has protective effect against liver hepatotoxicity, cardiovascular diseases, rheumatoid arthritis, diabetes, Alzheimer's disease and cancer¹⁰.

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Curcuma longa has a common name as HALDI. South Asia is a place where it is commonly found. It grows in twenty to thirty degree centigrade temperature and in abundant rain fall areas¹¹. *Curcuma longa* has polyphenols with yellow colour. It is quickly decomposed if exposed to high temperature, bright light and oxidative condition¹². It has an anti-inflammatory, anti oxidant and protective effect for liver against hepato toxic agent¹³.

MATERIALS AND METHODS

Thirty healthy rabbits were taken weighing between 2500-3500 grams. The animals were divided in to three groups. Each group, the blood samples were taken up, was divided in to ten animals (N=10). Group A was taken as control. It was on fresh Alfalf and tape water. Experimental Group B was given INH dissolved in fresh water morning and evening till twenty days while 10 mg of *curcuma longa* was added in last ten days. Group C was given *Curcuma longa* powder 100 mg with INH 50 mg per kilogram of body weight twice a day.

Fresh Alfalfa was given to all groups with fresh water. A male and female rabbit were together and was ad libitum. On day one, ten and twenty, the blood samples were taken from venous puncture of ear lobule of each animal.

The blood taken from ear lobule of rabbit is shifted to the centrifuge machine and centrifuged at the rate of 3000 rpm for twenty minutes. The Aspartate Amino Transferase (AST) in the serum was estimated by the Kits from Randox USA. Samples of liver were sent for histopathological evaluation.

RESULTS

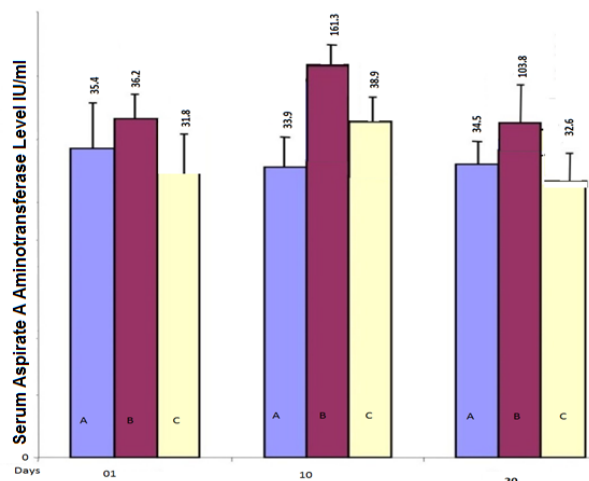
The liver enzymes were measured, which showed the liver toxicity was produced successfully by giving isoniazid 50mg/Kg of body weight twice a day. Aspartate aminotransferase in serum of first group A was 35.4 ± 8.09 IU/ml on day one, 33.9 ± 5.09 IU/ml on day ten and 34.5 ± 4.98 IU/ml on day 20.

Table No: 1 Changes in the Serum aspartate aminotransferase level

Serum aspartate aminotransferase level (AST) (normal range=14-113 IU/ml)				
Animal Groups	Day 1	Day 10	Day 20	P Value
Group A	35.4 ± 8.09	33.9 ± 5.09	34.5 ± 4.98	0.21
Group B	36.2 ± 7.57	161.3 ± 39.87	103.8 ± 25.71	0.01
Group C	31.8 ± 9.01	39.9 ± 8.73	32.6 ± 3.09	0.01

Group B has aspartate aminotransferase in serum as 36.2 ± 7.57 IU/ml on day 1, after giving INH the aspartate

amino-transferase level raised to 161.3 ± 39.87 IU/ml and on day 20 aspartate aminotransferase level was 103.8 ± 25.7 IU/ml, (10 mg of *curcuma longa* added in last ten days).



Graph No.1: Variations in AST Level in Rabbits after giving the INH in Group B and INH – *Curcuma Longa* Group C/ Group A is control on Alfa Alfa with fresh water.

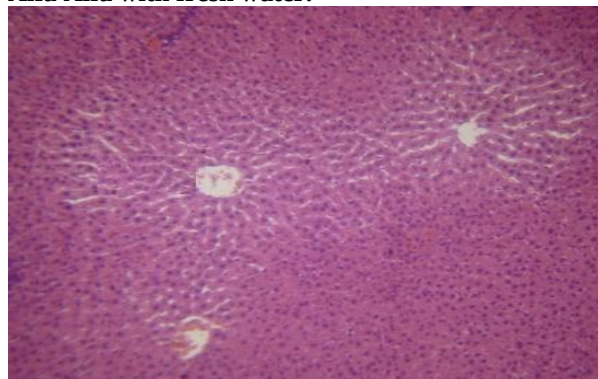


Figure No.1: Histology Pictures of normal lobe of liver of group A rabbits when they are on alfa alfa and fresh water H&E X 100.

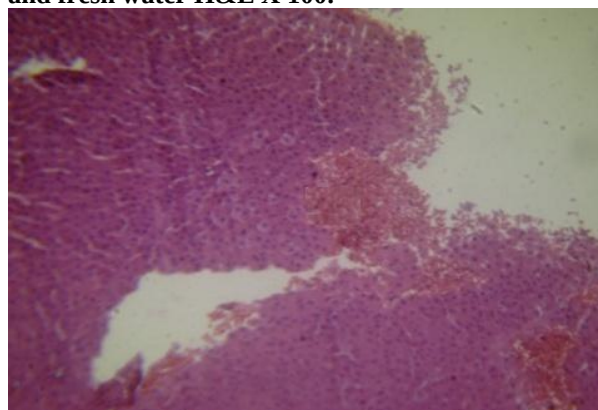


Figure No.2: Histological picture of lever hepatocytes disarrangement in group: B rabbits when given INH 50 mg/ kg/bw H&E X 100.

In last group C, aspartate aminotransferase in serum was 31.8 ± 9.01 IU/ml on day one, on tenth day, the level was 38.9 ± 8.73 IU/ml and on 20th day the level of the enzyme was 32.6 ± 309 IU/ml. The same results have been shown in Graph 1.

In group A, the arrangement of the hepatocytes are normal as is shown in figure 1. The dis-arrangement of the normal architecture of hepatocytes was observed in group B when INH 50mg/Kg has been given. The congestion of hepatocytes and hepatic necrosis can be observed in figure 2. The normal arrangement of the hepatocytes is regained when curcuma longa has been added to the rabbits in group C with INH, as has been given by figure 3.

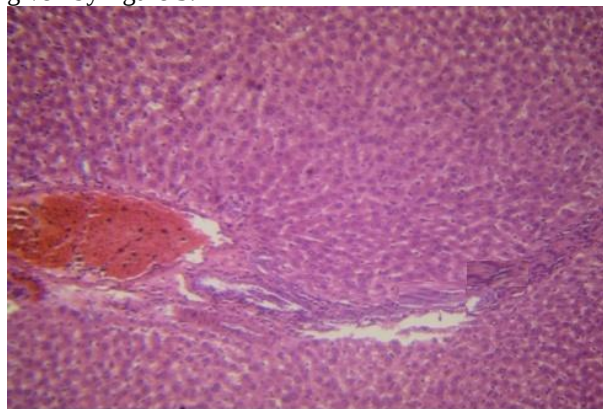


Figure No.3: In group C hepatocytes are arranged normally with INH + curcuma longa H&E X 100.

DISCUSSION

Liver, the largest gland of the body, has many chemical and important functions. It metabolized and detoxified many toxic substances coming in the body through our food. It is a store house for fat and certain vitamins¹⁴. Many drugs are capable to cause injury to liver others can lead to liver failure¹⁵. The idiosyncrasy of a drug to liver can lead to neither only hepatotoxicity but also to liver failure¹⁶. Liver is the place where all metabolism of all the drugs occurs¹⁷. The paranchyma of the liver can be damaged directly or inflammation may be there in the liver. Certain genetic and environmental factors can change the response of the liver¹⁴. In liver toxicity, the enzyme P 450 is released which is toxic for liver, then damage to the mitochondria is observed in hepatocytes. Now the deficiency of ATP is there and the different species of reactive oxygen accumulate in liver cells, causing more damage¹⁸. INH can damage the membrane of mitochondria, which can increase the permeability of mitochondria, releasing the cytochrome C, leading to cellular necrosis¹⁹.

Curcuma longa has protective effect against all the toxic agents of the liver. Curcumin has several group which function as antioxidant²⁰. It has been proved practically that curcuma longa is very effective against the Hepatotoxic agents.

CONCLUSION

The AST level has non significant changes in group A where P value was 0.21. The changes in group B and C are significant where P value in both were 0.01. In group B the AST level raised high during initial ten days where as AST level came down on day 20 probably due to addition of curcuma longa. The level of AST has remained close to normal in group C due to addition of high dose of curcuma longa. It does show the protective role of curcuma longa in Hepatotoxic drugs. The histopathological changes are visible in diagram after giving the INH and the reversal of it after giving the high doses curcuma longa. The damage of the liver paranchyma caused by isoniazid is reversed by adding the high dosage of curcuma longa.

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To Assess the Biogenesis of Lysine by *Penicillium Expansum* Using Agricultural Waste as Energy Source

Biogenesis of Lysine
by *Penicillium*
Expansum Using
Agricultural Waste

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ABSTRACT

Objective: To Assess the Biogenesis of lysine by *penicillium expansum* using agricultural waste as energy sources.

Study Design: Experimental study

Place and Duration of Study: This study was conducted at the CMH Institute of Medical Sciences Bahawalpur from May 2018 to September 2018.

Materials and Methods: The waste of Millet husk, sorghum husk and Banana stem were used throughout the study. Microorganism: *Penicillium expansum* was obtained from the Department of Botany, University of Glasgow, U.K. and was used in this study. The stock culture was maintained on agar slant, containing (G/L) dextrose 20: peptone 10: agar 20 and distilled water. The sterilized slants were inoculated with *penicillium expansum* and incubated at 27°C to obtain growth.

Results: In present study paper chromatographic method was carried out for separation and identification of amino acids synthesized by *penicillium expansum* in the culture broth using different solvent systems, which indicates that the selection of filter paper, solvent mixture and other conditions for paper chromatography are very important, because these determine R_f values and degree of separation.

Conclusion: This study concludes that biogenesis of lysine by *penicillium expansum* using agricultural waste as energy sources.

Key Words: Lysine, *penicillium expansum*, agricultural waste

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INTRODUCTION

Certain fungi are capable to synthesize amino acids¹. Amino acid synthesis capability of microorganism depends on the media composition, physical parameters and organism employed. The microbial synthesis of amino acids on an industrial scale has developed rapidly in the past decade. The impetus for these advances originated chiefly from the interest in the nutritional applications of lysine and other essential amino acids. It is judged that more than 600,000 metric tons of Lysine are fabricated annually and, unsettled to the utilization of new uses in pharmaceuticals, cosmetics and polymer materials, the market shows a growth potential of 7–10% per year.²

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Lysine application as a diet supplement in human being and domestic animals sought particularly in the under developed and over-populated area of the world where the chief staples are deficient in this amino acids, recently the production of lysine has received great interest as a consequence of the encouraging results obtained in feeding trials with cattle, dogs and poultry that are supplied a normal diet supplemented with lysine⁴. Lysine may be corresponding with indemnity against osteoporosis.⁵

L-Lysine has a known anxiolytic action through its effects on serotonin receptors in the intestinal tract. One study showed that overcharge of the 5-HT₄ receptors in the gut is integrated with anxiety-induced intestinal pathology.⁶ A study conducted in 2010 that addition with sufficient doses of Lysine could avert the development of Alzheimer Disease.⁷

Several European countries and South American countries are feeding the under nourished children with bread prepared with lysine as a nutritional supplement. Several commercial enterprises are employing lysine to fortify different cereal brands. Japan leads the world in microbial production of lysine. Only kyowa fermentation industry produces over 1000 tons of lysine per year.⁸

Selection of microorganism and cheapest nutritional media for the growth of microorganism and synthesis of desired amino acids is an essential parameter. Cultures

which are known for producing some quantity of essential amino acid are suitable sources and various methods can be used to enhance the production of amino acids¹¹. The present study was directed primarily towards the production of extracellular lysine by penicilliumexpansum using agricultural waste as a carbon source.

MATERIALS AND METHODS

In present study the waste of Millet husk, sorghum husk and Banana stem were used throughout the study.

Microorganism: Penicilliumexpansum was obtained from the Department of Botany, University of Glasgow, U.K. and was used in this study. The stock culture was maintained on agar slant, containing (G/L) dextrose 20: peptone 10: agar 20 and distilled water. The sterilized slants were inoculated with penicilliumexpansum and incubated at 27°C to obtain growth.

Degradation of millet, sorghum husk and Banana stem with 0.6N H₂SO₄: 10 g of millet, sorghum husk and Banana stem was separately mixed with 1000 ml of 0.6N sulfuric acid. These mixtures were frequently agitated on flame for one hour, maintaining the level of solution constant. After cooling at room temperature, the slurry was autoclaved at 1.5 kg/cm² for 30 minutes. The autoclaved slurry was cooled at room temperature and insolubilized material was removed by filtration through suction pump. The filtrate of solubilized millet, sorghum husk and banana stem was incorporated into the culture medium as a carbon source.

Culture medium: culture medium was used for the growth of penicilliumexpansum. Without altering chemical composition. Cultivation condition: 100 ml of culture media supplemented with millet, sorghum husk and banana stem soluble filtrate was taken in 500 ml conical flasks plugged with cotton wool and autoclaved at 1.5 kg/cm² for 20 minutes. The sterilized media cooled at room temperature were inoculated with 2.0 ml of penicilliumexpansum spores 50x per ml. These flasks were incubated in an orbital cooled shaking incubator (Gallenkamp) at 26±2°C adjust at 200 rev/min. The culture broth was separated from mycelium after an interval of 48 hours incubation period by filtration through whatman No. 1 filter paper.

Determination of mycelial biomass: The quantity of the mycelium was noted after washing with distilled water and drying at 105-110°C in a hot oven a constant weight was obtained.

Determination of final pH values: The final pH value of the culture broth was determined using WPA pH meter.

Amino acid analysis by paper chromatography: The amino acid were identified from culture broth by one and two dimensional paper chromatography. A 50 µl of culture broth and authentic samples as a marker were applied on whatman No. 1 filter paper. The paper strips were developed in the following solvent systems:

- A- Butanol-acetic acid –water (5:2:2) v/v/v).
- B- Ethanol- Ammonium hydroxide (2:2:1v/v/v)
- C- Chloroform –Methanol –Ammonium hydroxide ,
- D- Phenol-water 80:20 v/v),
- E- Propanol: water 7:3v/v)

In one dimensional procedure where as in the two dimensional, Butanol-acetic acid-water (5:2:2 v/v/v) and phenol –water (4:1 v/v) were used. After drying the chromatograms were sprayed with ninhydrin solution and dried in oven for five minutes at 80°C. Each spot was then identified by comparing with that of authentic amino acids.

Spectrophotometric determination of Lysine: Determination of lysine from culture broth: lysine was determined from culture broth of penicilliumexpansum according to the procedure of Kibrick.

RESULTS

Paper chromatographic method was carried out for separation and identification of amino acids synthesized by penicilliumexpansum in the culture broth using different solvent systems. Different R_f values were recorded with different solvent systems using one and two dimensional paper chromatography as shown in Table 1 & 2. Time course of lysine production by penicillium expansum using 0.6N H₂SO₄ pretreated millet husk and sorghum husk as a carbon source are presented in Table 3 and 4. However the production pattern of lysine by penicillium expansum on 0.6N H₂SO₄ pretreated banana stem waste mineral medium was found totally different than pretreated millet and sorghum husk mineral medium as presented in Table-5.

Table No. 1: R_f values (x100) standard acids and penicillium expansum culture amino acids by one dimensional paper chromatographic analysis using solvents from A to E.

Sr. No.	Amino acids	Rf in solvent A		Rf in solvent B		Rf in solvent C		Rf in solvent D		Rf in solvent E		
		Stand sample		Stand sample		Stand sample		Stand sample		Stand sample		
1.	Methionine	68	66	73	75\$	87	-	80	`81	72	72	--
2.	Lysine	22	--	21	62	-	83	81	38	-	12	--
3.	Alanine	47	--	--	59	56	86	-	61	62	47	--
4.	Glutamine	32	31\$	50	-	75	74\$	59	-	40	-	--
5.	Leucine	84	--	--	79	-	92	-	81	-	73	--
6.	Isoleucine	79	--	83	86\$	87	-	82	81	80	78	--
7.	Phenylalanine	80	--	82	86\$	94	-	81	--	87	-	--
8.	Arginine-	32	31\$	50	-	72	70\$	76	--	11	-	--

9.	Tyrosine-	60	-	68	-	83	-	65	--	57	57\$	--
10.	Tryptophan	70	-	65	-	85	-	77	-	68	64\$	-
11.	Threonine	40	93\$	51	-	91	-	65	-	42	-	-
12.	Histidine	29	-	36	-	85	-	72	73	30	-	-
13.	Glycine	32	-	31\$	59	-	85	-	45	44	48	-
14.	Asparagine	25	-	44	-	75	74\$	20	20\$	23	-	-
15.	Serine	30	-	31\$	38	40	85	-	39	-	30	-
16.	Valine	70	-	-	77	75\$	91	-	80	-	70	-
17.	Aspartic acid	28	-	30	-	73	-	20	20\$	32	-	-
18.	Glutamic acid	40	39\$	45	-	84	-	37	36	29	-	-
19.	Cysteine	48	-	-	52	-	86	-	60	-	44	-
20.	Cystine	16	-	14	32	-	70	-	24	25	16	-
21.	Proline	59	-	54	75	75\$	89	-	87	-	68	64\$

Table No.2: Rf values amino acids

Sr. No.	Amino acids	Rf value of standard	Rf values of broth amino acid phenol-water
1.	Methionine	77	71
2.	Lysine	30	28\$
3.	Alanine	62	60\$
4.	Glutamine	62	60\$
5.	Leucine	84	84\$
6.	Phenylalanine	84	84\$
7.	Asparagine	38	-
8.	Serine	29	28\$

9.	Valine	90	93
10.	Arginine	42	46
11.	Tyrosine	54	54
12.	Glutamic	30	28\$
13.	Cysteine	21	-
14.	Threonine	15	14
15.	Isoleucine	77	-
16.	Histidine	67	65\$
17.	Aspartic acid	14	14\$
18.	Tryptophan	80	84\$
19.	Glycine	29	46\$

Table No.3: Effect of pretreated Millet husk as a carbon source on the biosynthesis of lysine by penicillium expansum culture was grown at 28± 2°C in a cooled orbital shaking incubator.

Time Period Hours	Initial pH	final pH	Mycella weight g/100 ml broth	total protein mg/ml	reducing sugar mg/ml	lysine
24	6.0	5.67	0.585	2.84	0.023	2.00
48	6.0	5.94	0.65	2.6	0.024	2.00
72	6.0	7.34	0.585	2.08	0.019	2.90
96	6.0	7.85	0.405	0.36	0.018	2.80
120	6.0	7.8	0.4	0.155	0.016	2.80
144	6.0	7.7	0.4	0.11	0.014	2.80
168	6.0	7.77	0.4	0.1	0.014	2.80
192	6.0	7.75	0.4	0.1	0.009	1.20
216	6.0	7.72	0.4	0.095	0.008	1.20
240	6.0	7.7	0.4	0.095	0.007	1.20
264	6.0	0.07	0.4	0.085	0.006	1.20

Table No.4: Effect of pretreated sorghum husk as a carbon source on the biosynthesis of lysine by penicillium expansum. Culture was grown at 28±2°C in a cooled orbital shaking incubator.

Time Period Hours	Initial pH	final pH	Mycella weight g/100 ml broth	total protein mg/ml	reducing sugar mg/ml	lysine
24	6.0	0.126	0.55	2.84	0.026	2.00
48	6.0	0.146	0.62	2.4	0.023	2.40
72	6.0	0.177	0.55	2.6	0.018	1.44
96	6.0	0.199	0.405	0.86	0.018	1.40
120	6.0	0.113	0.345	0.8	0.018	1.40
144	6.0	0.106	0.33	0.75	0.015	1.40
168	6.0	0.103	0.325	0.09	0.015	1.40
192	6.0	0.102	0.325	0.075	0.014	1.40
216	6.0	0.098	0.295	0.075	0.013	1.40
240	6.0	0.095	0.285	0.065	0.012	1.20
264	6.0	0.09	0.215	0.065	0.012	1.20

Table No.5: Effect of pretreated banana stem waste as a carbon source on the biosynthesis of lysine by penicillium by penicilliumexpansum culture was grown at 28±2°C in a cooled orbital shaking incubator.

Time Period Hours	Initial pH	final pH	Mycella weight g/100 ml broth	total protein mg/ml	reducing sugar mg/ml	lysine
24	6.0	5.55	0.072	0.165	1.64	0.9
48	6.0	6.86	0.134	0.165	0.55	1.20
72	6.0	7.18	0.064	0.225	0.34	1.50
96	6.0	8.6	0.061	0.26	0.14	1.40
120	6.0	8.53	0.06	0.285	0.14	1.20
144	6.0	8.56	0.06	0.215	0.11	0.95
168	6.0	8.65	0.047	0.205	0.1	0.80
192	6.0	8.75	0.047	0.2	0.1	0.80
216	6.0	8.73	0.046	0.195	0.1	0.75
240	6.0	8.69	0.045	0.19	0.1	0.70

DISCUSSION

Different essential amino acids were found by the use of different solvents. These results are in agreement with the finding of stepka¹², who indicates that the selection of filter paper, solvent mixture and other conditions for paper chromatography are very important, because these determine Rf values and degree of separation.

It is observed that the amount of lysine production was increased upto 48 hours and then declined abruptly. It was noted that rise of pH was continuously in increasing order with increase of incubation period but the concentration of sugar and protein were found in decreasing order. These results are accordance with the finding of other workers in case of amino acid synthesis by bacteria, yeast and fungi on synthetic and natural media.

CONCLUSION

This study concludes that biogenesis of lysine by penicillium expansum using agricultural waste as energy sources.

Author's Contribution:

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Frequency and Outcome of Low Birth Weight Babies Admitted in Tertiary Care Hospital

Juverya Naqvi¹, Ali Akbar Siyal¹ and Tabinda Taqi²

ABSTRACT

Objective: To assess the incidence of LBW babies along with outcome and morbidity profile in our setup, as previously no such data is available.

Study Design: Retrospective study

Place and Duration of Study: This study was conducted at the Pediatric Ward of People's Medical College Hospital, Nawabshah from January to December 2016.

Materials and Methods: The data was extracted from file records of the patients admitted in NICU, regarding birth weight, their morbidity and mortality.

Results: Out of total admissions 4525 in NICU, low birth weight babies were 1177 (26%). Out of these 1177 babies 706 (60.11%) were male neonates and rest were females. The main reason for admission in these neonates were prematurity 439 (37.3%), sepsis 144 (12.23%), hypothermia and RDS 82 (7%), metabolic fits 42 (3.5%) and miscellaneous 65 (3%). The mortality was seen in 919 patients (43%).

Conclusion: Low birth weight was found in 26% of admitted neonates and associated morbidities included prematurity, sepsis, RDS, metabolic fits.

Key Words: Low birth weight, prematurity, Mortality, Nawabshah

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INTRODUCTION

Any baby's weight at birth is a chief indicator of its as well as the mother's health and nutrition during and before conception. By definition the low birth weight is weight at birth of <2500 grams¹. In year 2013, nearly 22 million newborns (16%) of all babies born worldwide that year had low birth weight. Exact estimation is quite difficult, because almost 50% of the world's newborns are not weighed at birth². Pakistan is in south Asian region and unfortunately the incidence of LBW babies is highest in this region, according to data from UNICEF, one out of four newborns babies has a weight less than 2500 grams², and as far as the outcome of such low birth weight babies is concerned, infants having <2.5 Kg weight are almost 20 times more die than good weight infants. According to Bhutta et al the incidence of low birth weight in Pakistan is around 32% out of total child births.

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Despite terrifying low birth weight situation in Pakistan, there is grim lack of research in this area³. It is documented that more than 20 million babies worldwide, and about 95.6% of them in developing countries are less than 2500 grams at birth. The %age of LBW in developing countries (16.5 per cent) is almost twice as in developed countries (7 per cent).² LBW cases babies are at an increase risk of complications at birth, and beyond, including hypothermia, hypoglycemia, sepsis, intraventricular hemorrhage, respiratory distress syndrome, patent ductus arteriosus, necrotizing enterocolitis and delayed complication including learning problems³. Low birth weight is a vast group of babies that include babies born before 37 complete weeks of gestation (preterm), intrauterine growth restricted babies, and sometimes even syndromic babies and babies affected by TORCH infection. Low birth weight is in most cases an outcome of poor maternal health and nutrition and thus there are many factors that are mostly related with intrauterine nutrition deprivation, along with decreased gestational age. Other risk factors associated with low birth weight are male gender, multiple pregnancy, ethnicity, delayed conception, advanced maternal age, maternal smoking, and babies with severe congenital deformities are reported in previous work^{5,6,9,10}. In another study the association of paternal factors like paternal age, education, employment, income and consanguinity was seen⁶⁻⁸. But these risk factors were not studied in this study.

MATERIALS AND METHODS

This is a retrospective study done at NICU of Pediatric Medicine Department of People's Medical College Hospital Nawabshah from January to December 2016. The newborn babies weighing less than 2500g admitted in neonatal care unit of our hospital were included in our study. The statistical tests used are percentages and proportions.

RESULTS

Out of total admissions 4525 in NICU, low birth weight babies were 1177 (26%). Out of these 1177 babies 706 (60.11%) were male neonates and rest were females. The main reason for admission are shown in table-1, in these neonates were prematurity 439(37.3%), sepsis 144 (12.23%), hypothermia and RDS 82 (7%), metabolic fits 42 (3.5%) and miscellaneous 65(3%). The mortality was seen in 919 patients (43%) (Fig-1).

Table No.1: Disease frequency for admission

S.No	Disease/Condition	Frequency and Percentage
1	Prematurity	439(37.3%)
2	Sepsis	144(12.23%)
3	Hypothermia+RDS	82 (7%)
4	Metabolic fits	42 (3.5%)
5	Miscellaneous	65(3%).

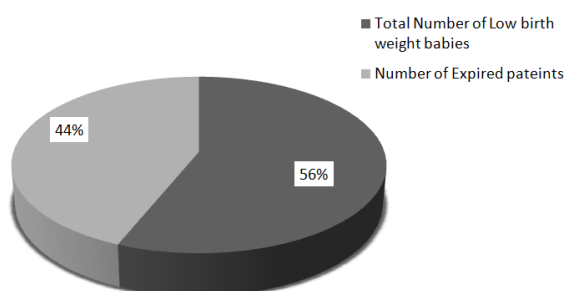


Figure No.1: Mortality percentages

DISCUSSION

We conducted this study at NICU of paediatric ward of PMCH Nawabshah to determine problems associated with LBW babies during their stay at hospital. Variations in incidence and characteristics of LBW reflects numerous risk factors and may be due to maternal malnutrition, medical illness, low income, insufficient knowledge about antenatal care and/or no antenatal care, scholastic, and ethnic backgrounds, while paternal risk factors like smoking, joblessness and many other that were not studied here but nevertheless have major impact on results^{11,12}.

In our study the frequency of LBW newborns was found to be 26% (1177 out of 4525, if we compare this to the incidence of LBW worldwide, it is 31% in South Asia followed by Middle East and North Africa (15%), Sub-Saharan Africa (14%) and East Asia and Pacific

7%¹³. In South Asian region the incidence of LBW is 36%, out of that 30% in Bangladesh and India respectively, and 19% in Pakistan¹³. A study from Peshawar shows that the overall incidence of low birth weight is 9.9%¹⁴, while a study from Abbotabad shows 30.3% much higher incidence compared to our set up¹⁵. The male to female ratio was 60:40, means a higher percentage of male babies as seen in other studies also¹⁶⁻²⁰.

The main reasons for admission in the low birth weight babies seen in our study was prematurity in 439 (37.3%) new WHO assessments of worldwide rate of preterm births indicate that of the 135 million live births in world during year 2010, 14.9 million babies were born before term, representing a preterm birth rate of 11.1%¹⁶. The high number of these before term births in Africa and Asia are linked, in part, to high fecundity and the huge number of births in these regions in contrast to other parts of the world¹⁶. The 10 countries with the highest numbers of estimated preterm births are India, China, Nigeria, Pakistan, Indonesia, United States, Bangladesh, the Philippines, Democratic Republic of the Congo and Brazil. These 10 countries constitute for 60% of all preterm births worldwide¹⁷. The fact that Mortality rates increase with decreasing gestational age, and babies who are both preterm and small for gestational age are at even higher risk is again well studied¹⁸. Next major reason for admission was sepsis, due to which 144(12.23%) babies were admitted that were low birth weight, internationally, it is estimated that more than 1.4 million neonatal deaths per annum are the consequence of invasive infections. Risk factors for early-onset neonatal sepsis (EOS) include prematurity, immunologic immaturity, maternal Group B streptococcal colonization, prolonged rupture of membranes, and maternal intra-amniotic infection¹⁹, and especially in low income countries risk of sepsis are increased. Hypothermia and RDS was the reason for seeking admissions in 82 (7%) patients in our setup, an international multicenter study shows that the RDS and sepsis to be the main reasons for morbidity and mortality in low birth weight babies²⁰, other reasons for admissions and in patient morbidity were metabolic fits in 42 (3.5%) and miscellaneous in 65(3%). In miscellaneous group in our study, newborns with congenital malformation and syndromes were included, Ismail et al study on premature and low birth weight neonates and their management at Shaikh Zayed hospital, Lahore reported that the proportion of preterm and LBW with congenital malformations was 7.3% as compared to 5.4% among remaining deliveries²¹. A study from Hyderabad²² show low birth weight in 37.4%, major problems diagnosed on the first day of life in that study included Birth asphyxia in 61 (25.7%), RDS in 50 (21.1), hypoglycemia in 33 (13.9%), hypothermia in 31 (13.1%), jaundice in 23 (9.7%) and congenital malformation in 15 (6.35%) babies and IVH

was diagnosed in only 2 (0.8%) babies on first day of life²². The mortality seen in our setup was 43%. Many studies have been conducted regarding morbidities and mortality in LBW babies showing increased mortality and same patterns of problems in LBW babies with decreasing gestational age and birth weight²³⁻²⁴. Study conducted in Peshawar reported 52.52% mortality in LBW babies with neonatal sepsis, birth asphyxia and respiratory distress syndrome contributing to 91% mortality in them²⁵.

CONCLUSION

Our study showed that LBW is an important risk factor for various complications including RDS, hypoglycemia, hypothermia, sepsis, IVH, NEC and congenital malformations. Frequency of these problems increased with decreasing gestational age and birth weight. this is highly recommend that health education of mothers including better nutrition, vaccination and antenatal care and strengthening of health care facilities at both community and facility levels should be done to overcome the burden of LBW.

Author's Contribution:

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 Revisiting Critically: Juverya Naqvi, Ali Akbar Siyal
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Early Re-Bleed in Patients with Fundal Varices Treated with Injection Cynoacrylate (Histoacryl®)

Asif. R. Zaidi¹, Muhammad Zubair² and Ali Hyder³

Early Re-Bleed with Fundal Varices Treated with Inj. Cynoacrylate

ABSTRACT

Objective: To determine the frequency of early re-bleed in patients with fundal varices treated with Injection Cynoacrylate (Histoacryl®).

Study Design: Descriptive case series study

Place and Duration of Study: This study was conducted at the Department of Gastroenterology-Hepatology, Shaikh Zayed Hospital, Lahore from April 2012 to October 2012.

Materials and Methods: 100 patients were recruited. Injection Histoacryl® was injected and volume of injection was not exceeded from more than 1ml at one site. Maximum number of injection did not exceed more than two per site. After the procedure patient was shifted to Gastroenterology Ward where he or she was observed for early re bleed and data was noted regularly for 5 consecutive days.

Results: Present study showed mean age of the patients was 48.4±10.8 years. Patient distribution by gender, there were 68 (68%) male and 32 (32%) female patients. Out of 100, 12% patient had early rebleed in patients with fundal varices.

Conclusion: The frequency of early re-bleed in patients with fundal varices treated with Injection Cynoacrylate (Histoacryl®) is low. It is suggested that more multi-center studies should be conducted on large sample size so that the exact frequency of early rebleed could be obtained.

Key Words: Portal hypertension, early rebleed, fundal varices, Injection Cynoacrylate.

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INTRODUCTION

Patients with portal hypertension having 20 % chance to get gastric varices¹. After esophageal varices (EV), Gastric varices (GV) are the most common cause of upper gastrointestinal (UGI) bleeding in patients with portal hypertension. Gastric varices (GV) are accountable for 10-30% of all variceal hemorrhage. Conversely, they tend to bleed more severely with higher mortality. Around 35-90% rebleed after spontaneous hemostasis. Approximately 50% of patients with cirrhosis of liver harbour gastroesophageal varices. Gastric varices are related with gastroesophageal (GOV1, GOV2) and isolated gastric varices (GV1, GV2)^{2,3}.

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Although, consequence of hemorrhage in variceal has improved over the past two decades, variceal hemorrhage is still the most serious complication of portal hypertension and chronic liver disease.^{4,5} Bleeding occurs less often from gastric varices than esophageal varices, it's about 70 to 90% for all variceal hemorrhage. Severe blood loss, high bleeding rate, and higher mortality rate leads to poor prognosis of gastric varices⁷. Due to poor prognosis, limited data is present for the best treatment for gastric variceal hemorrhage^{8,9}. Treatment done by endoscopic injection of sclerosants, endoscopic band ligation is an substitute for management of gastric varices.^{10, 11}

Various studies conducted to know the best endoscopic treatment for gastric variceal hemorrhage. It is found that endoscopic injection of N-butyl-2-cynoacrylate found more effective than other sclerosants. In gastric variceal band ligation, episode of rebleeding did not occur past 1½ years in patient of gastric variceal obliteration. Although, most optimal endoscopic treatment of esophageal hemorrhage is endoscopic variceal ligation but its safety and efficacy is unclear. The re bleeding rate of gastric variceal obliteration with Injection Cynoacrylate (Histoacryl®) is variable and ranges from 10% to 42%.¹²

The rationale of this study is to find out the frequency of early rebleed in patients with fundal varices treated with Injection Cynoacrylate (Histoacryl®). In this regard there is evidence of data in western world, but

scanty evidence from our population. Present study reveal basic information about frequency of early rebleed in patients with fundal varices treated with Injection Cynocrylate (Histoacryl®).

MATERIALS AND METHODS

This Descriptive cases series was conducted from April 2012 to October 2012 at Shaikh Zayed Hospital, Lahore. Patient having age between 15- 65 years with portal hypertension presenting upper gastrointestinal bleed and evidence of bleed from fundal varices were selected. 100 patients were enrolled after taking informed consent in writing from Gastroenterology Unit of Shaikh Zayed Hospital Lahore. Endoscopy was done by researcher himself. Olympus upper gastrointestinal video endoscope GIF 160 was used in the procedure. Sengstaken Blackmore tube was made available in case of uncontrolled bleeding during the procedure. Two needle catheters 21 G were kept in hand. The endoscopist, assistant and the patient were using goggles for eye protection. The prepared injection Histoacryl® 2cc (Histoacryl® 1cc plus lipiodol 1cc, 1:1 dilution) were taken in 2.5cc syringe. Histoacryl® was injected through needle catheter of 21G (needle length 4mm and diameter 0.8 mm). Injection tube of endoscope was lubricated with lipiodol. Scope was introduced into the patient and positioned into body of stomach. Then injector catheter was advanced through the biopsy channel with the scope retroflexed to bring the gastric varix into view. The injector catheter tip was brought into contact with the base of varix, needle was introduced into varix and (Histoacryl®) was slowly injected, followed by distilled water flush, volume limited to dead space volume (1.5cc) of the injection catheter. The needle was promptly removed from varix to prevent needle impaction into varix. Precaution was observed that during and 20sec after injection no suction is applied. Volume of injection did not exceed more than 1ml at one site. Maximum number of injection did not exceed more than two per site. After the procedure patient was shifted to Gastroenterology ward where he or she was observed daily for early rebleed and data was noted regularly for 5 consecutive days. This data was collected through a proforma attached.

RESULTS

Table No.1: Percentage of patient according to age groups (n=100)

Age (Years)	No. of patients	Percentage
20-30	7	7.0
31-40	20	20.0
41-50	30	30.0
51-60	34	34.0
61-65	9	9.0
Mean±SD	48.4±10.8	

Total duration of this stud was six months and during that time, 100 patients were recruited. Out of 100, mean age of patient was 48.4±10.8 years, 7 (7.0%) patients underline 20-30 years age group, 20 (20%) were 31-40 years, 30 (30.0%) were 41-50 years, 34 (34.0%) were 51-60 years and 9 (9.0%) were 61-65 years (Table 1). Out of 100, there were 68 (68.0%) male and 32 (32.0%) female patients (Table 2).

Table No.2: Percentage of patients according to gender (n=100)

Gender	No. of patients	Percentage
Male	68	68.0
Female	32	32.0
Total	100	100.0

Out of 100, 12% patients were frequency of early rebleed and 88% patients were not early rebleed (Table 3).

Table No.3: Percentage of patients according to their early rebleed (n=100)

Early rebleed	No. of patients	Percentage
Yes	12	12.0
No	88	88.0
Total	100	100.0

In the stratification of age with early rebleed, out of 100 only 1 (1%) patient of early rebleed was in 20-30 years and 31-40 years age group respectively, 2 (2%) patients was in 41-50 years, 5 (5%) patients in 51-60 years and 3 (3%) patients in 61-65 years (Table 4).

Table No.4: Stratification of age with early rebleed (n=100)

Age (Years)	Early rebleed			
	Yes		No	
	Number	%age	Number	%age
20-30	1	1.0	6	6.0
31-40	1	1.0	19	19.0
41-50	2	2.0	28	28.0
51-60	5	5.0	29	29.0
61-65	3	3.0	6	6.0
Total	12	12.0	88	88.0

In the stratification of gender with early rebleed, there were 8 (6%) male and 4 (4%) female patients in which early rebleed occurred (Table 5).

Table No.5: Stratification of gender with early rebleed (n=100)

Gender	Early rebleed			
	Yes		No	
	Number	%age	Number	%age
Male	8	8.0	60	60.0
Female	4	4.0	28	28.0
Total	12	12.0	68	68.0

DISCUSSION

Portal hypertension is related with the most serious complexities of cirrhosis, including ascites, hepatic encephalopathy, and leaking from gastro-esophageal varices. In spite of the advancement accomplished throughout the most recent decades, the 6-week mortality related with variceal draining is still in the request of 10–20%¹³.

Gastric varices eruption has the attributes of more serious blood misfortune and higher mortality and speaks to a harder issue than hemorrhage in esophageal variceal.^{14,15} The contributing fundamentals of GV are anatomical and specialized. Anatomically, gastro-esophageal varices (GV) lie further inside the submucosa than esophageal varices (EV), by and large are bigger than EV, deplete straightforwardly into wide veins, (for example, the gastroduodenal shunt) without interceding smaller veins (which empty the insurances out of EV), and are presented to corrosive and pepsin.¹⁶ Theoretically, analysis of GVH is more problematicas the gastric mucosal bends, blood put together in the fundus, and high posterior wall are unclear.

While infusion sclerotherapy has been connected to treat dynamic leaking from GV, its utilization in GVH is related with a high rebleeding rate and a nonstop need to fall back on careful mediation and in this way is viewed as just a transitory hemostatic measure.¹⁷ The achievement rate to control GVH by endoscopic infusion of N-butyl-2-cyanoacrylate seemed higher than different sclerosants as per past non-randomized trials.^{18,19} The upside of endoscopic variceal ligation for EVH has been reported and has been recommended as the treatment of decision for EVH.²⁰ The hemostatic impact of endoscopic gastrointestinal variceal ligation (GVL) for GVH seemed promising, yet proof is as yet restricted.²¹

Present study showed that mean age of the patients was 48.4±10.8 years, 68% male and 32% female patients. As similar with the study of Tan et al²² the mean age of the patients was 61.4±14.6 years, male were in higher than female patients.

In our study, 18% patients had early re-bleed with fundal varices treated with Injection Cynoacrylate (Histoacryl®). As similar with the study of Tan et al²² 22.4% patients had early rebleed treated with injection cynoacrylate.

In our study the achievement rate in regulatory active bleeding was 82%. As similar with the study of Tan et al² the achievement rate of GVO in regulatory active bleeding was 93.3%. Attainment such a huge population of active bleeding is not easy. To establish a conclusion of equivalent efficacy in regulatory active bleeding, a huge case numbers trial founded on active bleeding is necessary. The achievement rate of GVL was also similar to that of preceding studies^{22,23} but higher than the rate in Lo et al.'s study. Due to different

technical application, there is difference in achievement rate of bleeding^{24, 25}.

CONCLUSION

Frequency of early re-bleed in patients with fundal varices treated with Injection Cynoacrylate (Histoacryl®) was low. It is suggested that more multi-center studies should be conducted on large sample size so that the exact frequency of early rebleed could be obtained.

Author's Contribution:

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Snake Bite: Pattern and Prevalence in DHQ Hospital Barkhan Balochistan

Snake Bite: Pattern and Prevalence in Balochistan

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ABSTRACT

Objective: To examine the frequency and pattern of snake bite in District Barkhan Balochistan and its surrounding areas in Pakistan.

Study Design: Retrospective study

Place and Duration of Study: This study was conducted at the DHQ Hospital District Barkhan Baluchistan from 1st January 2010 to 31st December 2012.

Materials and Methods: In this study total 811 patients of both genders were included during the study period. Patients detailed history including age, sex, socio-economic status and residency, types of snakes identified, site of bite and time of bite to hospital visit time duration was examined.

Results: There were 492 (60.67%) males while rest 39.33% females, Mostly patients were ages 20 to 40 years. Most of the patients 96.92% of incidences prefer treatment from DHQ Hospital while 3.08% use the different modalities. 39.95% were bitten by Eristicophis, 10.97% Cobra, and 30.95% by viper and 18.13% Krait. Lower limb was the most frequent site of the snake bite (70.03%).

Conclusion: Snake bite is one of a important problem in this district. We also concluded that Anti-snake venom shows better result and early treatment after snake bite can reduce the mortality rate.

Key Words: Snake bite, Frequency, Anti snake venom (ASV), Snake types

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INTRODUCTION

Snake bite is the most common problem in worldwide and mostly incidences found in rural areas. About 1.9/100000 deaths are estimated annually from snake bite.¹ Mostly rural areas has high rate of snake bite because of lack of health facilities and low literacy level, due to these factors mortality rate is high in rural areas as compared to urban populated areas. Worldwide, there are four families of venomous snakes Atractaspididae, Elapidae, Hydrophildae and Viperidae and in these four families contain different five hundred species and the fifth family of venomous snakes the Colubridae has fourty species. It is reported that about two hundred species are most poisonous and caused high rate of mortality and severe complications.²

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In Pakistan, Cobra, Krait and viper are the most common poisonous snakes found mostly in rural areas.³ In rural areas the prevalence of snake bite cases is high and most of the deaths are recorded due to snake bite and the most common reason for high mortality rate is the delay in getting the victims to a well equipped medical health care center for better treatment and the 2nd most common reason is to use other treatment modalities. Most of the researches regarding snake bite reported that mostly cases of snake bite happen when the people working in theirs cultivating fields or when people sleeping in open area.⁴

The identification of risk factors associated with a fatal outcome of snake bite would be very helpful to better target intervention measures. Several previous studies described clinical and epidemiologic features of fatal elapid snake bites but none, to our knowledge, identified true risk factors of death by comparing groups of victims with fatal and non-fatal outcomes.⁵⁻⁸

In District Barkhan, where more than 90% of the population is engaged in agricultural activities and in summer rainy seasons mostly people were effected with snake bites. This hospital based study was conducted to examine the frequency and pattern of snake bites in people of District Barkhan and surrounding areas aimed to provide better and quick treatment and to aware people of early treatment and to reduce the mortality rate in this area due to snake bites.

MATERIALS AND METHODS

This retrospective study on the treatment of snake bite envenomation was conducted at DHQ Hospital District

Barkhan Baluchistan during the year 2010 to 2012. In this study total 811 patients of both genders who were visited first time to seek treatment for the snake bite were included during the study period. This Hospital has the better treatment facilities of snake bite such as Anti Snake Venom. Patients having history of previous snake bite treatment and those whom were bitten from other species except snake was excluded from this study. Patients detailed history including age, sex, socio-economic status and residency, types of snakes identified, site of bite, and time of bite till time to hospital admission was examined. All the statistical data was analyzed by SPSS 17.0.

RESULTS

Out of 811 victim's record of 319 (39.33%) females and 492 (60.66%) were males with ages 10 to 60 years. 191 (23.56%) patients had ages less than 20 years, 446 (55%) patients had ages 20 to 40 years and 174 (21.45%) were ages between 41 to 60 years. 642 (79.16%) patients had rural residency and 20.84% had urban residency. Most of the patients 571 (70.41%) patients had low social economic status while 29.59% had middle socio-economic status (Table 1).

Table No.1: Demographical details of all the patients

Variable	No.	%
Gender		
Male	492	60.67
Female	319	39.33
Age (years)		
< 20	191	23.55
20 – 40	446	55
41 – 60	174	21.45
Residency		
Urban	169	20.84
Rural	642	79.16
Socioeconomic status		
Low	571	70.41
Middle	240	29.59

Table No.2: Time to incidence to hospital visit

Time (hours)	No.	%
> 4	268	33.05
4 – 12	333	41.06
13 – 24	179	22.07
> 24	31	3.82

Most of the patients 96.92% of incidences prefer treatment from DHQ Hospital while 3.08% use the different treatment modalities. Time of incidence to time to visit hospital is the most important factor and was noted as < 4 hours, 4 to 12 hours, 13 to 24 hours and > 24 hrs as 268 (33.05%), 333 (41.06%), 179 (22.07%) and 31 (3.82%) respectively. 85% of the people know about the Anti Snake Venom (ASV) while 15% do not know about it. 39.95% were bitten by Eristicophis, 10.97% Cobra, and 30.95% by viper and

18.13% Krait. Lower limbs were the most common sites of the snake bite and found in 70.03%. In our study, 4 (0.49%) patients were died and those were visited hospital after 72 hours of snake bite (Tables 2-4).

Table No.3: Types of snake and site of snakes bite

Variable	No.	%
Type		
Eristicophis	324	39.95
Cobra	89	10.97
Viper	251	30.95
Krait	147	18.13
Site bite		
Lower Limb	568	70.03
Other	243	29.97

Table No.4: ASV given to patients and mortality rate

Characteristics	No.	%
ASV		
Yes	786	96.92
No	25	3.08
Mortality		
Yes	4	0.49
No	807	99.51

DISCUSSION

Worldwide, snake bite is the most significant problem and most of the cases reported in rural areas. In our study, we observe that snake bite incidences were most common in rural areas of District Barkhan Balochistan Pakistan as compared to urban areas. The main reason was most of the people was farmers and worked in the fields and in rainy season most of the cases reported with snake bites. Many of other studies regarding prevalence and patterns of snake bite reported that most of the cases were found in rural areas.⁷⁻⁹ In our study, mostly patients were ages between 20 to 40 years and the rate of male patients population was high as compared to females, these results was similar to some previous studies in which the main age range was 18 to 40 years and males patients rate was high as compared to females.^{10,11}

In our study we found 492 (60.67%) victims were male while 39.33% patients were females and most of the patients 70.41% had low socio-economic status. A study conducted regarding snake bite shows similar results.¹² In this study, mostly patients recognize the type of snake and only few patients didn't recognize due to darkness and fear. In the present study few of patients brought dead snake with him to the hospital. A study conducted on pattern of snake bite demonstrated that many of people brought dead snake specie to hospital for identification.¹³ this may helps to identify the snake species and the frequency of that species in this area. In recent study, Time of incidence to time to

visit hospital is the most important factor and was noted as < 4 hours, 4 to 12 hours, 13 to 24 hours and > 24 hrs as 268 (33.05%), 333 (41.06%), 179 (22.07%) and 31 (3.82%) respectively. We found that many of victims first consult with traditional practitioner and than visit to hospital. Many of other studies demonstrated that 80% of snake bite victims first consult with traditional practitioner and not to prefer the quick and timely visit to hospital.¹⁴⁻¹⁶

In our study, we found that 39.95% were bitten by Eristicophis, 10.97% Cobra, and 30.95% by viper and 18.13% Krait, these results shows similarity to other study in which Eristicophis, krait and viper was the most common type of snakes found in Pakistan rural areas.¹⁷ Patients who arrived late had higher severity scores, poor outcome and higher number of complications like renal failure, breathing difficulty, and cellulitis. In our study, 4 (0.49%) patients were died and those were visited hospital after 72 hours of snake bite. A study conducted by Bhatti et al in which mortality was found in 2 patients.¹⁸

In rural areas of Pakistan there is lack of medical facilities and it may also the main cause of delay in treatment and this major problem may lead to increase the mortality and morbidity rate. Moreover, Government should provide better facilities in these areas and there is a great need to be developed for the management of this problem.¹⁹

CONCLUSION

Snake bite is one of a significant problem in this population area. It is concluded that most of the patients were ages above than 20 years and eristicophis, krait and viper was the most common types of snakes found in this area. We also concluded that Anti-snake venom shows better result and early treatment after snake bite can reduce the mortality rate. Moreover, people must have to aware the ASV for better and quick treatment.

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Major Consequences, Determinants and Obstetrical Outcomes of Unintended Pregnancy

Determinants
and Obstetrical
of Unintended
Pregnancy

Farida Wagan¹, Ali Akbar Siyal², Raisham Ali¹ and Tabinda Taqi³

ABSTRACT

Objective: We aimed to study frequency, determinants and obstetrical outcome of unintended pregnancy.

Study Design: Cross sectional study

Place and Duration of Study: Gynecology and Obstetrics department, during May 2017 to October 2017.

Materials and Methods: This study was conducted at the Department of Gynecology and Obstetrics, PUMHS Nawabshah SBA from May to October 2017.

Materials and Methods: All pregnant women carrying singleton pregnancy of more than 28 weeks gestation were eligible while women with multiple pregnancy, alcoholics, smokers, and chronic diseases were excluded from the study. Determinants of un-intended pregnancy socio demographic variables as maternal age, educational and economic status, age at marriage, pregnancy related variables as gestational age in weeks, parity, birth interval, booking status, antenatal services and prenatal outcome as preterm birth, low birth weight, stillbirth were recorded.

Results: Unintended pregnancy was reported by 47% of women in our study. The following variables shows positive association with unintended pregnancy as maternal aged between 20-40 years, mostly with low education, having more than two births, birth interval less than 12 months, belongs to poor socio economic status, age at marriage less than 20 years, delayed prenatal care, belongs to rural areas while common prenatal outcome observe preterm birth and low birth weight.

Conclusion: This study concluded high percentage of unintended pregnancy with substantial negative consequences for women and her child, thus signifying need for effective and directed sex education and family planning facilities.

Key Words: Frequency, determinant, obstetrical outcome.

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INTRODUCTION

Unintended pregnancy is a significant issue in public health. An unintended pregnancy can be described as either unwanted or ill-timed pregnancy. Existing population of world is seven billion and developing countries account for its 97%. About 210 million conceptions annually occur worldwide and 75 to 80 million of these are knowledgeable to be unintended. Unintended pregnancy is a central model that is used to better know the rate of birth in a population and the unmet need for contraceptive method acting (birth ascendance) and family planning^[2,3].

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Unintended pregnancy is related with social and financial burden and maternal behaviors such as smoking, alcohol consumption and late beginning of prenatal care. Consequences of unintended pregnancy mainly from, not using contraception or unpredictable use of effective birth control device methods^[3]. Without the use of contraceptive during sexual activity, improper use of contraceptive method and failure of the method chosen are contributing factors of unintended pregnancy^[4]. The major consequences of unintended pregnancy are abortion, 88% of pregnancies ending in induced abortion due to unwanted pregnancy or contraceptive failure. Rate of unintended pregnancies seems to be ascending, as shown by recent study conducted by population council (a non-government organization) according to that, unintentional pregnancy rate increased between 2002 and 2012 from 71 to 93 per1000 women aged 15-49 (38%-46% respectively). In 2012, out of nine million pregnancies, 4.2 million were noted as unintended in Pakistan, including 54 % cases of induced abortion and 34% in unplanned births. The risk ratio of death in developing countries in comparison with developed countries is 25-250 times greater for a woman who undergoes an unsafe abortion. Major factors predicting unsafe abortions are structure of family, spacing in birth, socio economical status, mother well being, dearth, unemployment of spouse,

waged or working women, conflicts with spouse and so many others. Ample research work has been done on abortion as one of the complications of unintended pregnancy so we aimed to study determinants and other adverse fetal-maternal outcomes of unintended pregnancy.

MATERIALS AND METHODS

This was a cross-sectional study, conducted in the Gynecology and Obstetrics Department Unit I PUMHS, Nawabshah, during May to October 2017. After the ethical review committee of PUMHS approved permission was taken and written informed consent was gained from all the applicants. All women having singleton pregnancies with gestational age above 28 weeks were recruited, the ladies having established obstetrical complications like obstructed labor, eclampsia and persistent illness, cigarette smoker, alcoholics, multiple gestations, left out from study. All the demographic and other data was collected on a proforma designed for the study including socio demographic variables, factors related with reproductive health, contraceptive history and measure of unintended pregnancy. The intention of pregnancy was checked by LMUP. The LMUP comprising of six questions, each of which assesses different features of moods and events precede to pregnancy (as stopping use of contraceptive, conversing pregnancy with spouse and health behavior changes prior to getting pregnant). Each variable scored as 0, 1, 2 and score summed to attain a combined score between 0 and 12. Pregnancies then categorized as unplanned (score 0-3), ambivalent (4-9) or planned (10-12). Women with score less than 10 (ambivalent and unplanned) were well-thought-out as unintended.

RESULTS

We observed a total 2480 pregnancies having mean gestational age of 30 weeks. Overall unintended pregnancies were 1166 (47%), out of them unplanned were 670 (57.4%) and 496 (42.5%) were ambivalent, and remaining were intended. The majority 672 (57.6%) of women were having age between 20-40 years. More than half 792 (67.9%) were from rural population and about half of these were illiterate and belong to poor socioeconomic class. 54.8% of these had age less than 20 years at the time of marriage and majority 728 (62.4%) having birth interval < one year. Over all 85.3% cases had knowledge about at least one of the contraceptive method but 33.8% of women described using them. Among modern method of contraception, 96% had knowledge of pills, 90% condoms, 94% IUDs, 96% injectable, 84% implants, female sterilization 70%, male sterilization 54%, while among traditional method, knowledge about rhythm and withdraw method account for 12% and 45% respectively, whereas use of contraception reported to be low for condoms 24 %, pills 11%, injection 15%, IUD 5.2 %, implants 8.8% while rhythm and withdraw

Table No. 1: The London Measure of Unplanned Pregnancy (LMUP) Questions

Variable	Answer	Score
At the time of conception	Always use contraception	0
	Inconsistently used contraception	1
	Not use contraception	2
In terms of becoming a mother	Wrong time	0
	An OK time but not quite right	1
	Right time	2
Just before falling pregnant	Not intend to become pregnant	0
	Did not mind either way	1
	Intend to get pregnant	2
Just before falling pregnant	No want for a baby	0
	Have mixed feeling about having a baby	1
	Want a baby	2
Before falling pregnant had you and your partner	Never discussed children	0
	Discussed children but no firm agreement	1
	Agreed to pregnancy	2
Health actions before falling pregnant	No action	0
	1 action	1
	2 or more actions	2

Table No.2: Clinical and Demographic Data

Variable	Description	Number (%)
Pregnancy intention	Unintended (score <10)	1166 (47%)
	Intended (score >10)	1314 (52.98%)
Wealth index / socio economic status	Poor	550 (47%)
	Middle	230 (19.7%)
	High	386 (33%)
History of miscarriage / abortion	Yes	628 (53.8%)
	No	538 (46%)
Parity	>2	820 (70.3%)
	<2	346 (29.6%)
Gestational age	28-34 weeks	725 (62%)
	34-37 weeks	252 (21%)
	>37 weeks	189 (16%)
Maternal age	<20 years	212 (18%)
	20-40 years	672 (57.6%)
	>40 years	282 (24%)
Area of residency	Rural	792 (67.9%)
	Urban	374 (32%)
Educational status	Illiterate	580 (49.7%)
	Primary	120 (10.2%)
	Middle	105 (9%)
	Matric	124 (10.6%)
	Intermediate	110 (9.4%)
	Graduation	127 (10.8%)
Age at time of marriage	<20	640 (54.8%)
	>20	526 (45.1%)
Birth interval	<12 month	728 (62.4%)
	>12 month	438 (37.5%)
Knowledge about family planning method	Yes	995 (85.3%)
	No	171 (14.6%)
Ever used	Yes	395 (33.8%)
	No	771 (66%)

method reported 4.9% and 30% respectively. Familiarity about emergency contraception was 20% and only 18% had ever used it. Our study showed that only 15% of women with unintended pregnancy received 4 antenatal visits while only 33% received single antenatal visit. As far as perinatal outcome is concerned preterm birth accounts for 10.5% of pregnancies, LBW 5.6% while neonatal death was recorded in 0.5% of cases.

DISCUSSION

The frequency of unintended pregnancy is 48% in our study which is higher than the documented global prevalence¹, the previous literature shows 16% and 24% in PDHS 2006 and 2013^{2,3}, comparable to study conducted by Sethar et al (46%)⁴ these studies used a dichotomous scale where as we used six item LMUP^{5,6,7}. The prevalence of unintended pregnancy indicated by various studies from Ethiopia (23.5%)⁸, Sudan (30.2%)⁹, Iran (33.7%)¹⁰, Kenya (24%)¹¹, Nepal (26-38%)¹², Tanzania (45.9%)¹³ but lower than study by Papua New Guinea (49.4%)¹⁴, Ghana (70%)¹⁵. We observe that unintended pregnancy has an association with age between 20-40 years comparable to study by Ethiopia that shows 67% of study population between 25-34 years⁸ same finding was observed in other studies also¹⁶ while studies from Papua New Guinea¹⁴, Kenyan¹¹, Tanzanian¹³, reported the chances of unintended pregnancy in age less than 20 years. PDHS 2012-2013³ cleared that gap between total wanted fertility and observed fertility rate is high in the rural areas (1.1 in rural and 0.8 in urban areas) as we indicate that the risk of unintended pregnancy is common in rural areas as which is supported by the study of Lamina MA¹⁷. Education has a key role in prevention of unintended pregnancy, since schooling increases autonomy and decision making and increases economic independence. Each additional year of education means a 10% reduction in fertility, subsequent increase in contraception uptake (Presler-Marshall and Jones 2012). The illiterate women even may not recognize that they are pregnant until it has become too late, and they may not be able to negotiate with their partners with regards to safe sex, thus prone to have unintended pregnancy more comparatively.

As shown in our study, education score is poor (around 50%), unintended pregnancy frequency high (47%) also supported by other studies women who are unschooled were more likely to have unintended pregnancy^{18, 19, 20}. Older women generally have achieved desired family size therefore more likely than the younger ones to report the current pregnancy as unintended as seen in study conducted in Pakistan¹⁶, that unintended pregnancy found to be common among women with more than two kids, also seen in our study, women with parity more than two account for 62% of total unintended pregnancies comparable to other studies^{14, 15, 19, 21}, birth interval less than 12 years reported to be more common in our study (62%), also supported by studies^{14, 23, 24}. Our study found that contraception

knowledge is common but use is very low. Only 34% of women with unintended pregnancy use contraception. Risk of unintended pregnancy found to be double in women who never use contraception as compared to current users as it is consistent with the literature^{11, 14, 25, and 26}. Pregnancy intention seems to be affecting maternal desire of receiving maternal health services, women who are not intending to be pregnant may not recognize the symptom of pregnancy, in fact not be in optimal health for childbearing, as missed preconception care (which is known to reduce certain issues such as spina bifida) and are more likely to delay in seeking antenatal care, so less support for practicing healthy behavior such as quit smoking, alcohol cessation, and thus less preparation of parenthood, as seen in our study that only 15% of women receive antenatal care services more than 4 times and only 33% receive single antenatal service. This was also supported by study in Bangladesh²⁵ and Dibaba Y et al²⁶. In our study low birth weight was associated with early denial of pregnancy, as found in 5.6% of unintended pregnancy in our study, comparable to study by Mohlajee, APMPH et al (5.9%)²⁹ and by Hultin (5.6%)³⁰ while study by Morris (8.5%)³¹, Joycee (7.6%)³², Dourousseau (2.6%)³³ and by Bitto (3%)³⁴, suggest that patient with early rejection of pregnancy have twice the risk of preterm labor we saw 10.5% of the women with unintended pregnancy had preterm birth nearer to study by Pulley³⁵ (11.6%), Messer³⁶ (11.3%), Mohlajee²⁹ (9.5%), Flower A³⁷ (8.16%), while seems to be more prevalent in study by Orr³⁸ (15.5%).

CONCLUSION

This study highlights increased burden of unintended pregnancy and low use of family planning services and this is the fact for whole Pakistan and other under development countries though the complete eradication of all unintended pregnancy is an unrealistic goal. However appreciable reduction in the number of unintended pregnancies would improve the wellbeing of future generation. The fact that industrialized countries like Pakistan suggest that progress in desired direction is a realistic and feasible goal.

Author's Contribution:

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Conflict of Interest: The study has no conflict of interest to declare by any author.

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To Determine the Diagnostic Accuracy of 12 Lead ECG For Detection of Posterior Myocardial Infarction Keeping 15 Lead ECG as Gold Standards

Mushtaq Ahmad, Noorul Hadi, Shah Wali, Abdul Wali, Tajender

ABSTRACT

Objective: Predictive value of 12 lead ECG in the diagnosis of posterior myocardial infarction keeping 15 lead ECG as a gold standard.

Study Design: Cross Sectional Study

Place and Duration of Study: This study was conducted at the Department of Cardiology MTI Mardan Medical Complex, Mardan from February 2016 to August 2016.

Materials and Methods: Study was conducted in patients presenting with ST Segment elevation Myocardial Infarction. All patients meeting the inclusion criteria were enrolled in the study through OPD/ER department and were admitted in the ward for further evaluation. Patients were quickly evaluated by history and clinical examination and then immediately subjected to 12 lead ECG to detect the posterior MI. Immediately after completing the 12 lead ECG, additional 3 posterior leads were applied to detect posterior MI on 15 lead ECG. Data was entered on a well prepared proforma and SPSS Version 21 was used for analysis of data.

Results: In this study, 165 patients were observed in which mean age was 62 years with standard deviation ± 1.33 . 53% percent of the patients were male while 47% patients were female. Posterior myocardial infarction on 15 lead ECG among 165 patients was detected in 25(15%) patients and was not detected in 140(85%) patients.

Posterior myocardial infarction on 12 lead ECG among 165 patients was detected in 17(10%) patients and undetected in 148(90%) patients. Diagnostic accuracy of posterior myocardial infarction on 12 lead ECG, keeping 15 lead ECG as gold standard, had Sensitivity=60%, Specificity = 98.57%, Positive predictive value= 88.24%, Negative predictive value = 93.24%, and Diagnostic Accuracy 92.72%.

Conclusion: Our study concludes that the diagnostic accuracy of posterior myocardial infarction on 12 lead ECG was 92.72%. with sensitivity= 60.00%, specificity = 98.57%, positive predictive value= 88.24% and negative predictive value = 93.24%.

Key Words: Diagnostic Accuracy, 12 lead ECG, posterior myocardial infarction, 15 lead ECG

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INTRODUCTION

CAD is as big a Problem in Pakistan as in the rest of the world. CAD is a growing health problem world wide. it has implications for both men and women. By 2021, it is postulated to be the number 1 killer world wide.¹ Those in the lower socioeconomic strata suffer a worst outcome as compared to the rich. This disease entity deserves the most in terms of resources as it has a very high mortality and morbidity associated with it.^{2,3}

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Optimal care of these patients must be ensured. This would decrease the burden of the disease. We must adhere strictly to the standard guidelines in the care of these patients.⁴

According to the most careful estimates based on sound scientific studies nearly 100, 000 suffered an acute MI in Pakistan in the calendar year 2002⁵. MI has the different types like Anterior MI, Inferior MI, Right Ventricular MI and Posterior MI⁶.

Anterior MI has grave prognosis as it damages larger part of myocardium while isolated inferior MI damages only a small portion. But Inferior MI should not be taken inferior as it carries poor prognosis if associated with Right ventricular (RV) MI, Lateral or Posterior MI because it is associated with large area of myocardium of LV⁷.

Posterior Myocardial Infarction cannot be picked easily on 12 lead ECG because it has no direct relation with posterior wall, so has been phrased as dark side of moon⁸. ST segment depression in anterior leads has

been considered as mirror imaging of posterior wall (equivalent of ST segment elevation in posterior wall). But this doesn't truly exist in every case because ST segment depression in anterior leads has been considered as only electrical phenomenon in reciprocal leads or ischemia in anterior leads. $C^{7,8,9}$ should be done in emergency to look for association of posterior myocardial infarction. Any change in ECG except posterior leads is neither sensitive nor specific for posterior MI⁹. Increasing the number of leads even up to 80 leads further increases the sensitivity¹⁰.

Any clue for posterior MI on 12 lead ECG is an indication for posterior leads (15 lead ECG)⁷. This double practice ECG wastes golden time of thrombolytic therapy. An idea to cumulate all the clues of posterior MI and compare it with 15 leads ECG. Ten of 12 patients who has ECG changes on 12 lead ECG were confirmed to have posterior MI on 15 lead ECG¹¹. In another study, for diagnosis of posterior myocardial infarction, 43.3% sensitivity and 95.1% specificity was found in 12 lead ECG with an overall prevalence of posterior MI was 49%¹².

Very limited data is available on this scenario so the aim of this study is to determine the diagnostic accuracy of posterior MI on 12 lead ECG keeping 15 lead ECG as gold standard. In our settings, the burden of MI patients is very high and our staff is very busy. More than 1000 ECGs are performed in casualty and almost 500 ECGs inside Cardiology department. If we find the sensitivity and specificity of 12 lead ECG for detection of posterior MI to be significantly high as compared to available literature, we can use it as a routine in the detection of Posterior MI and the patient can be thrombolysed on early basis by saving the golden time for thrombolysis as saving minutes means saving muscles of myocardium.

MATERIALS AND METHODS

This study was performed at Department of Cardiology, Mardan Medical Complex, Mardan. It was a Cross Sectional(Validation) Study with a duration of 6 months from 29/02/2016 to 29/8/2016. The Sample size was 165 keeping 43% sensitivity, 95% specificity, 40% proportion of posterior myocardial infarction, 95% confidence interval and precision for sensitivity 10% and precision for specificity 4.5%. (n=165)

Data Collection Procedure: The study was initiated after due approval was accorded to it by the Research and Ethical Committee. The patients fulfilling the inclusion criteria were recruited. (i.e. those with characteristic ischemic chest pain, pain epigastrium, sweating, nausea and vomiting) were enrolled in the study. Patients in the OPD/ER who had changes on 12 lead ECG underwent further scrutiny in the ward. The purpose and benefits of the study was explained to all patients and they were assured that the study is done

purely for research and data publication and if agreed a written informed consent was obtained.

All patients were quickly evaluated for history and clinical examination. All patients were immediately subjected to 12 lead ECG to detect the posterior MI on the basis of criteria mentioned in operational definitions. Immediately after completing the 12 lead ECG, additional 3 posterior leads were applied to detect posterior MI on 15 lead ECG keeping in view the criteria mentioned in operational definitions.

All the patients were immediately managed as per ward protocols. All ECG recordings and reports were done under supervision of an expert cardiologist. The results of the study were compiled in the form of Graphs and Charts. All data were entered into a proforma.

Data Analysis: SPSS version 21 was used for data analysis. Mean + standard deviation was calculated for age while Frequency and percentage were calculated for gender. Sensitivity, Specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy was determined by taking 15 lead ECG as gold standard. Effect modifiers including age and gender were controlled through stratification. Statistical Analysis was done by using chi square test. All the results were presented in the form of tables or charts.

RESULTS

In this study a total of 165 patients, attending Department of Cardiology Mardan Medical Complex, Mardan were observed to determine the predictive value of 12 lead ECG in the diagnosis of Posterior Myocardial infarction, keeping 15 lead ECG as gold standard. The results obtained as:

For the different age groups, 165 patients was analyzed as 36(22%) patients were in age range 41-50 years, 63(38%) patients were in age range 51-60 years and 66(40%) patients were above 61-70 years of age. Mean age was 62 years with standard deviation ± 1.33 .

Gender distribution among 165 patients was analyzed as 87(53%) patients were male while 78(47%) patients were female.

Detection posterior myocardial infarction on 15 lead ECG among 165 patients was detected in 25(15%) patients and was not detected in 140(85%) patients. (as shown in Table 1)

Detection posterior myocardial infarction on 12 lead ECG among 165 patients was detected in 17(10%) patients and was not detected in 148(90%) patients. (as shown in Table 2)

Diagnostic accuracy of posterior myocardial infarction on 12 lead ECG keeping 15 lead ECG as gold standard was analyzed as 12 lead ECG had Sensitivity= 60.00%, Specificity = 98.57%, Positive predictive value= 88.24%, Negative predictive value = 93.24%, Diagnostic Accuracy = 92.72%. (as shown in Table 3)

Table No. 1: Posterior myocardial infraction on 15 lead ECG (n=165)

15 Lead ECG	Frequency	Percentage
Detected	25	15%
Not detected	140	85%
Total	165	100%

Table No. 2: Posterior myocardial infraction on 12 lead ECG (n=165)

12 lead ECG	Frequency	Percentage
Detected	17	10%
Not detected	148	90%
Total	165	100%

Table No. 3: Posterior myocardial infraction on 12 lead ECG vs 12 lead ECG (n=165)

		Posterior MI on 15 Lead ECG		
		Detected	Not Detected	Total
Posterior MI on 12 Lead ECG	Detected	(A) 15 TP	(B) 2 FN	17
	Not Detected	(C) 10 FP	(D) 138 TN	148
	Total	25	140	165

Sensitivity= 60.00%

Specificity = 98.57%

Positive predictive value= 88.24%

Negative predictive value = 93.24%

Diagnostic Accuracy = 92.72%

DISCUSSION

Posterior Myocardial Infarction cannot be picked easily on 12 lead ECG because it has no direct relation with posterior wall, so has been phrased as dark side of moon⁸. ST segment depression in anterior leads has been considered as mirror imaging of posterior wall (equivalent of ST segment elevation in posterior wall). But this doesn't truly exist in every case because ST segment depression in anterior leads has been considered as only electrical phenomenon in reciprocal leads or ischemia in anterior leads. C7, 8, 9 should be done in emergency to look for association of posterior myocardial infarction. Any change in ECG except posterior leads is neither sensitive nor specific for posterior MI⁹. Increasing the number of leads even up to 80 leads further increases the sensitivity^{10,11}.

In this study 165 patients were observed and categorized as follows; 22% patients were in age group 41-50 years; 38% in age group 51-60 years and 40% were above 61-70 years of age. Mean age was 62 years with standard deviation ± 1.33 . Fifty three percent patients were male while 47% patients were female. Diagnostic accuracy of posterior myocardial infarction on 12 lead ECG keeping 15 lead ECG as gold standard

was analyzed as 12 lead ECG had Sensitivity= 60.00%, Specificity = 98.57%, Positive predictive value= 88.24%, Negative predictive value = 93.24%, and Diagnostic Accuracy = $15+138/165 * 100 = 153/165 * 100 = 92.72\%$.

Similar results were observed in another study conducted by Din I et al¹¹ in which a total of 176 patients were observed. The predicted value of 12 lead ECG was found to be 55, using 15lead ECG as gold standard for Posterior MI. 12 Lead ECG has an accuracy for all age groups, as well as men and women alike.

A previous study using 15-lead ECG in comparison with 12-lead ECG showed equivalent results. The sensitivity and positive predictive value of 12-lead ECG for the diagnosis of MI was around 90%. Similarly, the specificity for MI was also around 90%. A 15 lead ECG added only very little to the findings on 12 lead ECG.¹²⁻¹⁶ Our study showed similar results.

A 12 lead ECG is a cheaper modality for the diagnosis of Posterior Myocardial infarction. V789 are valuable leads in case of a 15 lead ECG. Its sensitivity and specificity is around 90%.^{17,18,19} Wall motion abnormalities for the diagnosis of Posterior Myocardial Infarction have been used in earlier studies. However sensitivity and specificity is less than that of ECG.^{20,21,22} Nevertheless, wall motion abnormality on Echocardiography can have a collaborative evidence in the diagnosis of infarction.

CONCLUSION

Our study concludes that the diagnostic accuracy of posterior myocardial infraction on 12 lead ECG was 92.72%. with sensitivity= 60.00%, specificity = 98.57%, positive predictive value= 88.24% and negative predictive value = 93.24%.

Author's Contribution:

Concept & Design of Study: Mushtaq Ahmad
 Drafting: Noorul Hadi
 Data Analysis: Shah Wali, Abdul Wali, Tajender
 Revisiting Critically: Mushtaq Ahmad, Noorul Hadi
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Conflict of Interest: The study has no conflict of interest to declare by any author.

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Prevalence of Varicella Zoster Virus Infection in Renal Transplant Recipients; A Single Centre Study

Varicella Zoster
Virus Infection in
Renal Transplant
Recipients

Syed Munib¹, Ahmad Zeb Khan², Najmuddin¹ and Mufti Baleegh Ur Raheem Mahmood²

ABSTRACT

Objective: Varicella zoster virus (VZV)-related disease, particularly herpes zoster, is important infective viral complication of renal transplantation due to long-term immunosuppression. In our study we examined the clinical presentation, prevalence and outcome of herpes zoster virus in post renal transplant patients.

Study Design: Retrospective / cross-sectional study

Place and Duration of Study: This study was conducted at the Institute of Kidney Diseases Peshawar (both as in-patient and out-patient department) from August, 2010 to July, 2018.

Materials and Methods: A cross-sectional retrospective study design was followed in this research in which medical record files of all the patients who underwent renal transplant at Institute of Kidney Diseases (IKD) Peshawar were reviewed.

Results: n=8 subjects (3.33%) developed herpes zoster during a follow-up of 8 years post-transplant. Mean time to the development of VZV infection was 2.27 years (ranging from 06 month to 4.16 years). All patients in cohort had presented with single dermatomal distribution of lesions, none of the patients developed disseminated disease or post herpetic neuralgia.

Conclusion: VZV is a common complication after renal transplantation, but in our study the prevalence was very low i.e. 3.3%. Prompt diagnosis and treatment prevent the complication of VZV and visceral disease. Pre transplant active immunization for VZV negative patients should be done to prevent VZV infection.

Key Words: Renal Transplantation, Varicella zoster virus infection, Mycophenolate Mofetil

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INTRODUCTION

Varicella-zoster virus (VZV) is a double-stranded DNA virus member of the herpes virus family. VZV also has the ability to establish lifelong latency in cranial nerve or dorsal nerve root ganglion after primary infection and persist in the infected host for life.¹

VZV is the second most common viral infection in solid organ transplant (SOT) recipients (after cytomegalovirus), with a prevalence of about 29%.^{1,2} While, zoster occurs in approximately 11% of SOT recipients within four years of transplant due to long term immunosuppressive therapy.^{2,3,4} An increased incidence of zoster were reported among SOT recipients used Mycophenolate Mofetil.^{5,6} Herpes zoster classically occurs in the first 6 months after

transplantation in SOT recipients; however it can manifest clinically longer after transplant. VZV infection in adult renal transplant recipient results from reactivation rather than primary infection with severe sequel occurs.^{6,7} Reactivation disease (herpes zoster or shingles) occurs with an annual incidence of 1.5-3.0 cases/1000 in general population and is clearly age related with incidence rising to 10 cases/1000 in subjects over 65 years of age.⁸ The incidence in SOT recipient is 10-100 folds higher than general population ranging from 1-12%.^{9,10}

The most common clinical manifestation of varicella zoster virus reactivation is cutaneous HZ, involving usually less than two adjacent dermatome, however atypical clinical findings, disseminated disease, visceral involvement and lethal outcome has been described.¹¹ In addition 20-40% of transplant patients will acquire post-herpetic neuralgia as a secondary complication, considerably greater than the rate in immunocompetent population.¹²

After the primary episode, VZV remains dormant in cranial nerves and dorsal root ganglia and potentially can revive up to decades later as zoster (shingles).^{13,14} Zoster is more commonly observed in older age recipients and those individuals having decreased cell mediated immunity.⁸⁻¹⁴

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MATERIALS AND METHODS

A cross-sectional retrospective study design was followed in this research in which medical record files of all the patients who underwent renal transplant between August 1st, 2010 and July 31st, 2018, at Institute of Kidney Diseases (IKD) Peshawar were reviewed. Demographic, clinical and laboratory information of the patients were gathered from the medical files including age, gender, dialysis duration, duration of transplantation, type of donor, immunosuppression protocol, episodes of allograft rejection, pre-transplant VZV status, distribution of VZ, complications, treatment given and outcome of treatment.

All the renal transplant recipients had received antiviral prophylaxis according to their documented cytomegalovirus (CMV) status, while all the transplant recipients received induction with interleukin-2 receptor (IL-2R) antagonist (Basiliximab).

Maintenance immunosuppression constituted of triple regimen selecting either a Calcineurin inhibitor (Tacrolimus or Cyclosporine), or anti-proliferative drug (Mycophenolate sodium MPA, or Everolimus (mTORi) with oral prednisolone.

RESULTS

Medical record of 250 patients was reviewed during the study period. Those patients who were lost to follow up after 3 months were excluded. Finally 240 patients were considered for further study with mean age of 34.408 ± 8.306 year, and were further followed for a period of 39.51 ± 10.37 months. The characteristics of these patients are shown in Table 1.

Table No.1: Characteristics of renal transplant patients (n=240).

Characteristics		n (%)
Age at transplantation	Less than 40 years	174 (72.5)
	More than 40 years	66 (27.5)
Gender	Male	182 (75.8)
	Female	58 (24.2)
Follow-up time (months) mean	39.516 ± 10.371	
Deaths at last follow up	No	240 (100)
	Yes	0 (0)
Rejection	No	216 (90)
	Yes	24 (10)
Pre-transplant Varicella Zoster Disease	No	218 (90.8)
	Yes	22 (9.2)
Post-transplant Varicella Zoster Disease	None	232 (96.7)
	Single Dermatome	8 (3.33%)

Majority of the patients, about 75.8% (n=182), were male, and 27.5% (n=66) of the patients were above age of forty year at the time of transplantation. About 9.2% (n=22) patients had pre-transplant Varicella zoster virus disease. Almost 10% (n=24) patients had an episode of either acute or chronic rejections during the follow up period.

All patient received maintenance immunosuppression during the follow up period, 62.9% (n=151) received Cyclosporine and Mycophenolate Mofetil (CSA + MMF), while rest received either Tacrolimus and Mycophenolate (TAC + MMF) or Cyclosporine and Everolimus (CSA + EVERO). The frequencies of immune suppression used in patient are shown in figure 1. Out of these n=240 renal transplant patients, 3.33% (n=8) patients showed post-transplant Varicella zoster virus infection. And all had only single dermatomal involvement. There were no recurrence and none of the patient had disseminated disease. No death has been reported as a result of VZV infection. All of the affected patients were treated with oral antiviral acyclovir as outpatient and all recovered completely.

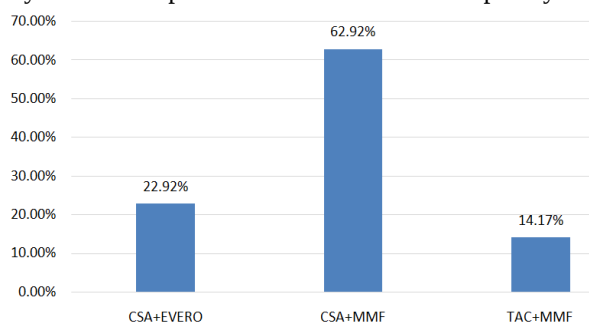


Figure No.1: Frequency of Maintenance Immunosuppression

DISCUSSION

VZV is the 2nd most common viral infection in post renal transplant patients after cytomegalovirus (CMV). A variety of complications of VZV has been noted in different studies worldwide with unfavorable outcomes.⁶ The prevalence of VZV in our study was 3.33% which is lower than in comparison to other studies which have reported higher prevalence of VZV.^{2,3,9,15,16} Our study findings revealed that VZV infection were higher in male while other study showed VZV predominance in female.¹⁷ All the patients who developed VZV infection had a history of the VZV infection before renal transplant and none of them received vaccination for VZV.

The prevalence and severity of the VZV infection is related to the intensity of the immunosuppression including induction, maintenance and anti-rejection therapy.^{15,18,19}

Although MMF inclusion to the transplant treatment protocols has improved the graft survival but on other hand it has increased the prevalence of different viruses like VZV or CMV.^{2,20} All our patients with VZV were

on MMF based regime with induction therapy with Basliximab and had received anti-rejection therapy. All the patients were found to involve only single dermatome. There was no case of disseminated disease; additionally no case of post-herpetic neuralgia was reported in our study. All the cases were managed with oral administration of acyclovir 800mg thrice daily for ten days with reduction of MMF dose with complete recovery and no relapse was observed.

The limitation of our study is being retrospective, single center study and also low sample size. No pre-transplant VZV serology status records were present in our study. But despite all these above limitation our study is the real first to study the prevalence, risk factors, complications, treatment and outcome of VZV infection in post renal transplant patients in Pakistan.

CONCLUSION

VZV infection is frequent viral infection in post renal transplant patients in our center after CMV infection. Intense immunosuppression (induction, maintenance and anti-rejection) is a risk factor for VZV infection despite use of universal viral prophylaxis.

Recommendations: VZV serology should be done before renal transplant and all seronegative patients should be vaccinated before transplantation. This will decrease the prevalence of VZV infection in our renal transplant recipients. Prompt treatment with acyclovir and reduction of MMF dose is cost effective treatment for VZV infection in renal transplant patients.

Author's Contribution:

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Conflict of Interest: The study has no conflict of interest to declare by any author.

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To Compare Prophylactic Zinc Supplementation Versus Placebo in Terms of Frequency of Diarrhea in Infants of 6-11 Months

Prophylactic Zinc
Supplementation Vs
Placebo for
Diarrhea in Infants

Sobia Noor¹, Sohail Ashraf¹, Sommaya Siddiqua², Saba Mushtaq¹ and Munazza Saleem¹

ABSTRACT

Objective: To compare prophylactic zinc supplementation versus placebo in terms of frequency of diarrhea in infants of 6-11 months.

Study Design: Randomized control trial study

Place and Duration of Study: This study was conducted at the Outpatient Department of Pediatrics, POF Hospital, Wah Cantt from March 2016 to September 2016.

Materials and Methods: Non Probability Consecutive sampling was used to enroll children and was divided into two groups by lottery method as control group receiving placebo and case group receiving the supplemental zinc. The case group was then given 5ml of syrup containing 20 mg of elemental zinc daily for 2 weeks followed by 6 months of follow-up. The control group was given placebo. At each follow-up, the mother/caregiver was asked about the occurrence of diarrheal episodes and duration of diarrhea during the previous month.

Results: Total of 120 children were included in the study and divided into two equal groups. In group A (control group) mean age 8.23 months and SD ± 1.37 . In group B(case group) mean age 8.02 months and SD ± 1.17 . In group A minimum diarrhea episode was nil, maximum diarrhea episodes were 15 with mean diarrhea episodes 8.53 and SD ± 3.15 . In group B minimum diarrhea episode was nil, maximum were 9 with mean diarrhea episodes 5.13 and SD ± 2.73 .

Conclusion: Diarrhea is a common disease in developing countries with significant morbidity and mortality. Results of the current study show significant reduction in diarrheal morbidity in infants even 6 months after short-course of zinc prophylaxis.

Key Words: Diarrhea, Placebo, Zinc

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INTRODUCTION

Zinc has a pivotal role in multiple cellular tasks and the immune system depends on the sufficient availability of this micronutrient¹. Regular dietary zinc consumption is needed because zinc can neither be produced nor stored². Inadequate dietary consumption and diarrheal diseases associated with negative zinc balance may contribute to deficiency of zinc which can lead to growth retardation and immune dysfunction^{3,4}. Zinc deficiency is prevalent in developing countries, including Pakistan^{4,5}.

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This is because the staple foods commonly consumed in these countries are deficient in zinc and rich in phytates which further impede zinc absorption and utilization^{1,5}. Diarrheal diseases are a significant health problem in developing countries⁶. There are 1.5 billion episodes of diarrhea per year and 21% of all deaths in children younger than 5 years are caused by diarrheal diseases⁷. Diarrhea is a major cause of death in children under 5 years of age in Pakistan, contributing 20-30% of these deaths. In a study from Egypt, Pakistan, Bangladesh, and Ethiopia report that 43% to 78% of deaths from diarrhea among children occur in the first year of life⁸. There was 23% reduction in mortality due to diarrhea and 19% reduction in incidence of recurrent diarrhea after zinc supplementation when given in suspension form⁹ or dispersible form¹⁰ during acute stage.

Similarly prophylactic zinc also results in significant reduction in the incidence of diarrheal diseases among infants³. Another study shows a 13% reduction in the incidence of diarrhea with preventive zinc supplementation⁴. Malik et al studied the effect of preventive zinc supplementation on diarrheal morbidity in infants 6-11 months and reported a 39% reduction in episodes of diarrhea, 39% in the total number of days

that a child suffered from diarrhea, and reduction of 36% in duration per episode of diarrhea¹.

To date, there is no published literature in Pakistan regarding the role of prophylactic zinc supplementation among infants in reducing the incidence as well as severity of diarrheal diseases. Because the incidence of diarrhea is higher in children 6-12 months of age¹, the purpose of this study was to evaluate the role of zinc in reducing diarrheal morbidity by short course prophylactic supplementation to infants aged 6-11 months. The results of this study will help to consider the prophylactic zinc supplementation to infants in a diarrhea prevalent country like Pakistan.

MATERIALS AND METHODS

This Randomized control trial was done at Outpatient Department of Pediatrics, POF Hospital, Wah Cantt from 1st March 2016 till 30th September 2016 and Non Probability Consecutive sampling technique was used. Sample size was calculated by using WHO formula 2.2a with following values:

Level of significance = 5%

Power of test = 80%

Anticipated population proportion₁, $P_1=80\%^2$

Anticipated population proportion₂, $P_2=95\%^2$

Required sample size is 60 infants in each group.

a) Inclusion criteria:

- Infants with age ranging from 6 to 11 months visiting outpatient pediatric department of POF hospital for vaccination or healthy siblings.
- Either gender.

b) Exclusion criteria:

- Any infant receiving zinc supplement at the time of study
- Any infant who had received zinc supplement in the preceding 3 months
- Those who were severely malnourished, immune-deficient or currently on steroid therapy
- Those who are severely ill requiring hospitalization,
- Families likely to migrate from the study area

Operational Definitions:

Diarrhea: Diarrhea was defined as 3 or more watery stools in a 24 hour period within 6 months of zinc supplementation.

Short Course Zinc Supplementation: Oral zinc preparation containing 20 mg elemental zinc/5ml given in a dose of 5ml once daily for 14 days

Data collection Procedure: Permission from the hospital ethics committee was sought before the commencement of the study. Informed consent was obtained from parents/guardians for inclusion in the study. All children 6-11 months of age fulfilling the above mentioned inclusion criteria were enrolled in the study by first year postgraduate residents. The enrolled

children were divided into groups by lottery method as control group receiving placebo and case group receiving the supplemental zinc. Demographic features such as age and gender were asked and noted on a specially designed performa.

A baseline assessment was done at the time of recruitment, which included weight and length measurements. The case group was then given 5ml of syrup containing 20 mg of elemental zinc daily for 2 weeks followed by 6 months of follow-up. The control group was given placebo. Follow-up for diarrhea began on the 15th day after intervention. Each child was followed-up monthly by phone calls and the follow-up was continued for 6 months after the completion of zinc supplementation. To ensure that the child did not receive additional doses of zinc, mothers were provided identity cards indicating the study title. These cards were to be produced whenever the child is taken to any medical practitioner. At each follow-up, the mother/caregiver was asked about the occurrence of diarrheal episodes during the previous month.

Data Analysis Procedure: The data was entered and analyzed using SPSS version 16. For continuous variables such as age and diarrheal episodes; mean $\pm$ SD was calculated. Frequencies and percentages were measured for categorical variables such as gender and frequency of episodes of diarrhea. To compare frequency of diarrhea between two groups chi-square test was applied. $p\text{-value} \leq 0.05$ was considered as significant.

RESULTS

Total of 120 children were divided into two equal groups. In group A minimum age of patients was 6 months, maximum age was 11 months with mean age 8.23 months and SD ± 1.37 . In group B minimum age of patients was 6 months, maximum age was 11 months with mean age 8.02 months and SD ± 1.17 . There was predominance of female patients in the study (Table 1). In group A maximum diarrhea episodes were 15 with mean diarrhea episodes 8.53 and SD ± 3.10 . In group B maximum were 9 with mean diarrhea episodes 5.13 and SD ± 2.73 .

Table No.1: Demographic Data

Characteristics	Group A (control) (n-60)	Group B (case) (n-60)	Total (N-120)
SEX:			
• Male	26 (43%)	25 (42%)	51(26.2%)
• Female	34 (57%)	35 (58%)	69(34.2%)
AGE CATEGORY:			
• 6-7 months	19 (31.6%)	20 (33.3%)	39(32.5%)
• 8-9 months	32 (53.3%)	34 (56.6%)	66(55%)
• 10-11 months	9 (15%)	6 (10%)	15(12.5%)

In group A there were 56(93%) patients with diarrheal episodes and in group B there were 49(82%) patients with diarrheal episodes (p-value 0.0001). Zinc supplementation had significant effect on patients between 8-9 months of age (p-value- 0.016). (Table 2).

Table No.2: Effect of Zinc and Placebo

(1) Gender:		Presence of Diarrheal Episodes		p-Value
		Yes	No	
Male	Group A (n-26)	25 (96.1%)	1 (3.8%)	0.087
	Group B (n-25)	20 (80%)	5 (20%)	
Female	Group A (n-34)	31 (91.1%)	3 (8.8%)	0.253
	Group B (n-35)	29 (82.8%)	6 (17.1%)	
(2) Age category:				
6-7 months	Group A (n-19)	17 (89.4%)	02 (10.5%)	0.957
	Group B (n-20)	18 (90%)	02 (10%)	
8-9 months	Group A (n-32)	31 (96.8%)	01 (3.1%)	0.016
	Group B (n-34)	26 (76.4%)	08 (23.5%)	
10-11 months	Group A (n-9)	08 (88.8%)	01 (11.1%)	0.756
	Group B (n-6)	05 (83.3%)	01 (16.6%)	

DISCUSSION

Zinc deficiency is associated with growth retardation and impairment of immune function, changes that are reversed when zinc is provided. In clinical conditions with severe zinc deficiency, or in animal experiments with zinc depletion, diarrhea is consistently found and responds quickly to zinc supplementation¹¹.

A clinical trial in an urban slum of Karachi, studied the effect of the daily use of micronutrients for two months on diarrhea in 6-11 months infants compared to placebo¹² and found decreased prevalence of diarrhea in children receiving zinc whereas in our study, this effect was seen after 2 weeks of supplementation. In another study in which zinc was supplemented for 7 months 23 % reduction of zinc morbidity was found with more effect in children less than 5 years of age¹³.

The response to zinc was equal in males and females in our study as also seen by Larson et al⁵ although Garenne et al¹⁴ had found zinc to be more effective in males. This effect has been attributed to difference in immune function between sexes.

In a similar trial of infants aged 6 to 11 months there was a 39% reduction in episodes of diarrhea, 39% in the total number of days that a child had diarrhea, and reduction of 36% in duration per episode of diarrhea

during the 5 months of follow-up¹. Similarly zinc has also been seen to reduce the number of stools per day¹⁵. The current study is limited to the frequency and number of episodes of diarrhea. The effect on the duration of each episode and types of diarrhea still needs to be studied.

In a community-based study, a birth cohort of 100 Low birth weight infants was randomly allocated into either an intervention group receiving zinc in vitamin B complex-based syrup or a placebo group receiving vitamin-based syrup from birth up to 1 completed year of age. The group which received zinc had diarrheal incidence of 1.36 episodes per child per year, whereas it was 1.93 episodes per child per year among the placebo group. Significant differences were present in linear growth and weight between the supplemented and placebo groups at the end of 1 year¹⁶. Another meta-analysis showed increase in length of 0.37 (±0.25) cm after zinc was supplemented for 24 weeks¹⁷. The current study has not studied the effects of zinc on linear growth and weight. However, this can be studied in future trials.

In a study in which children of 6 to 30 months were randomized to receive daily zinc gluconate during the 4 months of follow-up, a lower incidence of diarrhea was seen in the group who received zinc as compared with the placebo group¹⁸. In our study in the placebo group there were 56(93%) patients with diarrheal episodes while in zinc group there were 49(82%) patients with diarrheal episodes.

In another trial in which various children were given multivitamins, median percentage of days of diarrhea was less in children taking Vitamin A and zinc as compared to other children¹⁹. In a Tanzanian study, daily zinc supplementation of infants beginning at 6 weeks of age lowered the burden of diarrhea but provision of multivitamins did not confer additional benefit²⁰.

The major limitation of this study is that serum zinc levels were not measured to assess the deficiency and the subsequent effect on serum zinc levels after zinc supplementation. Studies in populations of Delhi have shown high prevalence of zinc deficiency²¹. Becquey et al²² in their study had found more increase in serum zinc level and reduced diarrhea incidence in the children receiving prophylactic zinc as compared to the children who took it only as therapeutic agent.

Moreover, the current study was done in a population that had not received zinc supplementation for the preceding 3 months and was apparently healthy. This coupled with the fact that the maximum burden of diarrhea is seen in the age group of 6 to 11 months²³ may have been responsible for such significant results in the current study. The intervention evaluated in the current trial is simple and inexpensive and can be incorporated into existing diarrheal disease control efforts.

CONCLUSION

Diarrhea is a common disease in developing countries with significant morbidity and mortality. The benefit of zinc given as a community-based prophylactic intervention is that it will decrease the incidence of diarrhea in the community compared with zinc supplementation during acute diarrheal episodes. Moreover, many children may not come to a health facility, especially in the slum populations, and thus keep suffering from repeated episodes of diarrhea. More studies need to be done to study the efficacy of zinc supplementation in diet so that more detailed observations can be done.

Author's Contribution:

Concept & Design of Study: Sobia Noor
 Drafting: Sohail Ashraf, Sommaya Siddiqua
 Data Analysis: Saba Mushtaq, Munazza Saleem
 Revisiting Critically: Sobia Noor
 Final Approval of version: Sobia Noor

Conflict of Interest: The study has no conflict of interest to declare by any author.

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Pattern and Frequency of Congenital Heart Diseases in Children with Down's Syndrome

Farman Ullah Burki, Taj Muhammad and Fazal Rehman

ABSTRACT

Objective: Congenital heart disease is a significant morbidity in children with Down's syndrome, the most prevalent chromosomal anomaly. The aim of this study is to determine the frequency and pattern of congenital great diseases in children with Down's syndrome in District Head Quarter teaching Hospital D.I.Khan.

Study Design: Descriptive Hospital based study

Place and Duration of Study: This study was conducted at the Department of Pediatrics, DHQ Teaching Hospital D.I.Khan from July 2016 to June 2017.

Materials and Methods: Fifty Eight(58) phenotypically Down's syndrome children That Presented to pediatrics department age 2 days to 14 years were included in study. Children more than 14-years age, Children with Congenital heart Disease without Down's Syndrome and normal children were excluded from study. Detailed data analysis including History, physical examination was done and there were subjected to 2 dimensional echocardiography.

Results:- Congenital heart diseases were found in 34 (58%) out of 58 patients. Among the affected patients, 21 (61.76%) were male, 13(38.2%) were female with male to female ratio 1.5: 1. Atrioventricular canal defect was the most common heart disease 12 (35.7). Followed by Fallots Tetralogy in 8 patient (23.52%), Ventricular septal defect 5 patient (14.7%) while combination of ventricular septal defect with pulmonary stenosis and patent Ductus Arteriosus in 5(14.71%) and least common disease was Isolated patent Ductus Arteriosus 4 patients (11.7%).

Conclusion: Congenital heart diseases are common in Down's syndrome. The commonest one is Atrioventricular canal defect followed by Fallots Tetralogy. All children with Down's syndrome should have a cardiac evaluation at birth.

Key Words: Down's syndrome, Congenital Heart Disease, Atrio Ventricular canal defect.

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INTRODUCTION

Down's syndrome is the most prevalent autosomal chromosome anomaly in live born neonates. Down's syndrome is defined by Trisomy of chromosome 21 in 95% cases and translocation or mosaic in 5% cases.^{1,2,3} It is the most common cause of moderate mental retardation and almost all patients have cognitive impairment with wide range of severity.⁴

Approximate incidence of Down's syndrome is 1 in 700-750 live birth while its prevalence rate is of 0.7 per 1000 births.^{5,6}

Down's syndrome is responsible for 4.9% of all congenital heart Diseases.⁷

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Down's Syndrome is characterized by Several clinical features including upslanting palpebral fissure, Epicanthic folds, depressed nasal bridge and cardiac anomalies as the most common congenital defects which occurs in 40-60% of patients and carries poor prognosis if not treated properly and timely.^{2,8,9}

The most common congenital heart diseases in Down's syndrome include atrial ventricular septal, Atrial septal defect, Tetralogy of Fallot, and Atrio Ventricular canal defect which is regarded as a characteristic cardiac anomaly in such patients.^{10,11} In Down's syndrome as Congenital heart diseases impose greater risk on patients, parents and health care system, knowledge of its epidemiology and prevalence in every geographical region is important as there is evidence that cardiovascular malformations may vary Based upon geography, ethnicity, and environmental factors.^{9,11,12}

This study was conducted to evaluate frequency and pattern of congenital heart disease in Down's syndrome district head Quarter Teaching Hospital Dera Ismail Khan of Khyber Pakhtunkhwa province

MATERIALS AND METHODS

This Hospital based descriptive study was carried out in Department of pediatrics, District Headquarter Hospital

Dera Ismail Khan from July 2016 to June 2017 over a period of one year. 58 (fifty eight) Down's Syndrome children aged 2-days to 14 years, diagnosed on basis of phenotypic appearance were randomly selected over the above mentioned period, irrespective of clinical or X-rays, findings of CHD. Detailed history and examination was performed in all patients and all were subjected to 2 dimensional echocardiography. In addition routine tests like CBC X-rays chest and ECG after written consent was obtained from the parents. Children more than fourteen years age, Children with Congenital heart Disease without Down's syndrome and normal children without Clinical features of Down's Syndrome were excluded from study.

All children were diagnosed as Down's syndrome on basis of their phenotypic feature like mongoloid faces, depressed nasal bridge, Low set ears, Upslanting eyes with epicanthic folds, transvers single Palmar crease, hypotonia and delayed milestones.

RESULTS

In 58 patients with Down's syndrome, 37(63.8%) were male and 21(36.2%) were female with male to female ratio of 1.6:1. The youngest patient was 15 days and oldest was 14 years old. Congenital heart diseases were found in 34 (58%) out of 58 patients. Among the affected patients, 21(61.76%) were male, 13 (38.2%) were female with male to female ratio of 1.5:1. The most common CHD was AV canal defect found in 12(35.7%) out of 34 patients followed by Tetralogy of Fallots in 8 (23.52%) out of 34 patients. Ventricular septal defect in 5% (14.5) and combination of Ventricular septal defect with pulmonary stenosis and Patent Ductus Arteriosus in 5(14.5%) and of 34 patients, and the least common was Isolated Patent Ductus Arteriosus in 4 (11.7%).

Table No.1: Type and Frequency of Congenital heart disease in Children and Down's syndrome.

S.No	Types of cardiac defect	No	Percentage
1	Atrioventricular canal defect	12	35.7%
2	Tetralogy of fallots	8	23.52%
3	ventricular septal defect	5	14.7%
4	Multiple lesions VSD+PS+PDA	5	14.7%
5	Patent duofus Artenoses	4	11.4%
	Total	34	100%

■ Atrioventricular canal defect ■ Tetralogy of fallots
 ■ ventricular septal defect ■ Multiple lesions VSD+PS+PDA
 ■ Patent duofus Artenoses

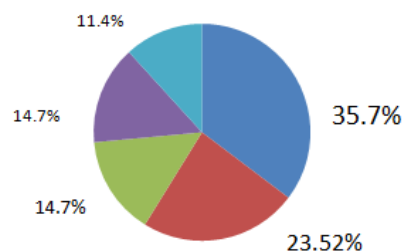


Figure No.1: Pie Diagram Showing Percentages of Congenital Heart Diseases

DISCUSSION

The presence of high incidence of CHD in Down's syndrome is well known fact. Many authors and literatures have published figures on frequency of congenital heart disease in Down's syndrome. These figures vary from 35 to 80% in different studies.¹³⁻¹⁷ The frequency of CHD in our study is 58 percent which is quite comparable to these studies.

The most common type of congenital heart disease in our study is Arterio ventricular canal defect (35.7%). This finding is similar to Irani, Indian, Lebanese, Caucasians and Sudanies children, where Arterio ventricular canal defect is the most common CHD accounting for 35 to 50 percent.^{17,18,20} But is different from findings in Saudi Arabian, Chinese and some local children's^{21,22}.

The frequency of Arterio ventricular canal defect in our study is very close that reported in India (28%), Nigeria (50%).^{11, 15} In our study Atrio ventricular canal defect was present in 35.7% children with Down's syndrome, this is similar to that reported by Ali et al (48.1%),²¹ Freeman et al, (45%)²⁴, Ashraf et al (28%)²⁵, Asim et al (50%)²⁶, and Okeniyi et al (54.7%)²⁷. but it was different from that reported by Khan et al (19.4%)²⁸.

The frequency of ventricular septal defect in Down's syndrome in our study was 5 (14.7%) and it was second most common congenital heart disease in our study. It is lower that reported by other workers^{28,29}.

In our study Patent Ductus Arteriosus was least common congenital heart disease that was present in 4 patient (11.5%) which is quite different from studies of other workers from Guatemala and Saudi Arabia where Patent Ductus Arteriosus is the most common congenital heart disease with frequency 28.6 and 47.8% respectively³⁰⁻³¹.

The most striking feature of our study was the high frequency of cyanotic congenital heart disease that is Fallots Tetralogy in Down's syndrome in 8 patient (23%), this frequency is quite high from that in Caucasians (6%),^{24,28} Saudi Arabians (5.3%),²³ but was somewhat similar to that reported by other workers Lo NS et al (6%),²² El Elmagrpy Z, et al (6.2%).³²

Congenital Heart Diseases in Down's syndrome tend to be single but may be multiple. In Our study isolated

Congenital Heart Diseases represented 85% of all the Congenital Heart Diseases in Down's syndrome Compared with 65% in Libya, 80% in Guatemala, 74% in Mexico and 78% in Turkey.³²

Our study has some limitations. This was single center study and not population based and diagnosis was made on clinical ground and no cytogenetic studies were carried out. So we could not comment on a frequency of CHD in different chromosomal alterations of Down's Syndrome.

CONCLUSION

Congenital Heart disease is common in Down's Syndrome Children. The most common congenital heart disease in Down's Syndrome is AVSD and VSD respectively. All children with Down's Syndrome should have cardiac evaluation with Echocardiograph in first week of life.

Author's Contribution:

Concept & Design of Study: Farman Ullah Burki
 Drafting: Taj Muhammad
 Data Analysis: Fazal Rehman
 Revisiting Critically: Farman Ullah Burki, Taj Muhammad
 Final Approval of version: Farman Ullah Burki

Conflict of Interest: The study has no conflict of interest to declare by any author.

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Frequency of Dyslipidemia in Patients Having Subclinical Hypothyroidism

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ABSTRACT

Objective: To determine the frequency of dyslipidemia in patients having subclinical hypothyroidism.

Study Design: Descriptive / cross sectional study.

Place and Duration of Study: This study was conducted at the Naseer Teaching Hospital Peshawar from Aug 2017 to Aug 2018.

Materials and Methods: The total sample size was 136 patients presenting with subclinical hypothyroidism taking 34.31% proportion of dyslipidemia in subclinical hypothyroid patients, 95% confidence interval and 8 % margin of error; using WHO software for sample size calculation. More over consecutive (non-probability sampling) technique was used for sample collection.

Results: In this study mean age was 40 years with SD 1.26. Sixty-three percent patients were female and 37% patients were male. Seventy percent patients had dyslipidemia while 30% patients didn't have dyslipidemia.

Conclusion: The current study shows that the incidence of dyslipidemia was found in patients having subclinical hypothyroidism.

Key Words: dyslipidemia, subclinical, hypothyroidism

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INTRODUCTION

Thyroid hormone by binding to the thyroid hormone receptors affects metabolism and growth in nearly all tissues of the body.¹ Thyroid hormones play vital role in the synthesis and metabolism of lipids.¹ The reduced secretion of thyroxine (T4) and triiodothyronine (T3) from the thyroid gland results in hypothyroidism.² The subclinical hypothyroidism (SH) is term used for the condition in which there is small elevation of thyroid stimulating hormone (TSH) in the presence of normal thyroid hormone levels. Disorders of thyroid gland are the second most common endocrine abnormalities globally after diabetes mellitus.³ An international study results showed that the prevalence of SH was 4.3% in general population, it also showed age and sex dependence.⁴ In another study it is reported that the prevalence of SH in general population is 4.3 - 9% and 16% in elderly females.⁴ In a national study, conducted among type 2 Diabetes Mellitus patients, 7.8% had SH⁵.

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The abnormalities in the lipid profile is a known complication of primary hypothyroidism dyslipidemia in turn increases the risk of hypertension and cardiovascular diseases.^{6,7} The aim of this study is to determine the frequency of dyslipidemia in SH patients in our setup. This hasn't been studied in our setup especially the dyslipidemia in patients having SH. The knowledge of the frequency of dyslipidemia in patients with SH in our setup will enable us to detect and treat dyslipidemia early and reduce the overall cardiovascular risk in such patients.

MATERIALS AND METHODS

This study was conducted at Naseer Teaching Hospital, Peshawar. Duration of the study was one year and the study design was descriptive cross sectional study. The total sample size was 136 patients presenting with SH taking 34.31% proportion of dyslipidemia in subclinical hypothyroid patients 12, (95%) confidence interval and 8% margin of error; using WHO software for sample size calculation. More over consecutive (non-probability sampling) technique was used for sample collection. All patients of SH not taking thyroxin or anti lipids drugs, patients of either gender and patients of age 18-60 years were included while hypothyroid patients on treatment, clinical hypothyroidism, ischemic heart diseases, renal disease, hepatic disease, Type 1 and type 2 diabetes mellitus, patients taking anti-lipids drugs, history of alcoholism, pregnancy were excluded from the study. The above mentioned conditions act as confounder and if included had introduce bias in the study result. All patient meeting the inclusion criteria and presenting with SH as per operational definition

were included in the study. All patients were worked up with detailed history, clinical examination and investigations like Thyroid function tests (TFTs), Fasting lipid profile (FLP), fasting blood sugar (FBS), Renal function tests (RFT), Liver function tests (LFT) and also relevant investigations to rule out other contributing factors for dyslipidemia in these patients. All the investigations were sent to the main pathology laboratory of Naseer Teaching Hospital, Peshawar. FLP and FBS were performed after overnight fasting. Detailed interview and data collection was done. The exclusion criteria were strictly followed to control confounders and exclude bias in study result. All the results were recorded in a pre-designed proforma. Data was analyzed by using Statistical Package for Social Sciences (SPSS) version 16.0. Mean + standard deviation was calculated for continuous variables like age of patients. Frequency and percentages were calculated for qualitative variables like gender, dyslipidemia. Dyslipidemia was stratified among age, gender and thyroid status to see effect modifiers. Results were presented as tables.

RESULTS

In this study 136 patients were observed in which 34(25%) patients were in age ranged from 21-30 years, 38(28%) patients were in age ranged from 31-40 years, 41(30%) patients were in age ranged from 41-50 years, 23(17%) patients were in age ranged from 51-60 years, Mean age was 40 years with SD 1.26. Eighty-six 63% patients were female and 50(37%) patients were male. The incidence of dyslipidemia was found to be 70% in our setup.

Table No. 1: Age Distribution (N=136)

AGE in (Years)	Frequency	Percentage
21-30 Years	34	31%
31-40 Years	38	33%
41-50 Years	41	36%
51-60 Years	23	17%
Total	136	100%

Table No.2: Gender Distribution (N=136)

Gender	Frequency	Percentage
Female	86	63%
Male	50	37%
Total	136	100%

Table No.3: Frequency of Dyslipidemia in Subclinical Hypothyroidism (N=136)

Dyslipidemia	Frequency	Percentage
Yes	95	70%
No	41	30%
Total	136	100%

Stratification of dyslipidemia with age distribution was analyzed as in 95 cases of dyslipidemia 24 patients were in age ranged from 21-30 years, 28 patients were

in age ranged from 31-40 years, 27 patients were in age ranged from 41-50 years, 16 patients were in age ranged from 51-60 years. Chi square test in table 4, the P value was 0.8996 and Chi square test in table 5, the P value was 0.6773.

Table No.4: Stratification of Dyslipidemia with Age Distribution (N=136)

Dyslipidemia	21-30 Year	31-40 Years	41-50 Years	51-60 Years	Total
Yes	24	28	27	16	95
No	10	10	14	7	41
Total	34	38	41	23	136

Table No.5: Stratification of Dyslipidemia with Age Distribution (N=136)

Dyslipidemia	Male	Female	Total
Yes	36	59	95
No	14	27	41
Total	50	38	136

DISCUSSION

Subclinical hypothyroidism (SH) is more frequent in areas of iodine sufficiency as compared to iodine deficient areas. The burden of SH in KPK is expected to increase with increasing iodine sufficiency. Studies have shown conflicting results concerning not only the degree of lipid changes in SH but also the effect of thyroxine substitution therapy. The effects of thyroxine replacement on lipid levels are not completely understood. Dyslipidemia is defined as the abnormal amount of lipids [total cholesterol (TC), low density lipoprotein cholesterol (LDL-C), high density lipoprotein cholesterol (HDL-C) and triglyceride (TG)] in the blood.⁸ The normal values are TC (< 200 mg/dl), LDL-C (<100 mg/dl), HDL-C (>60 mg/dl) and TG (<150 mg/dl).⁸ Hypothyroidism is an important cause of secondary dyslipidemia.⁹ In a local study, the prevalence of dyslipidemia among general population was 59.1%.¹⁰ Our study shows that the mean age of the patients was 40 years with SD 1.26. Sixty-three percent patients were female and 37% patients were male. Similar results were found in other studies as the mean age of patients in SH groups are 38.76±11.82 years, suggesting that mean age of patient's hypothyroidism seeking healthcare is around 40 years. These persons are more prone to cardiovascular complications and other problems. If treatment and other lifestyle interventions are initiated at a proper time these complications can be delayed, if not fully corrected. In the present study majority of the subjects i.e. 57%, 60%, 70% respectively in SH were females. These findings suggest that hypothyroidism is much more prevalent in the female population. Our study shows that the frequency of dyslipidemia in patients having SH was 70%. Similar results were found in study done by LU L et al¹⁵ in which the frequency of dyslipidemia in patients having SH was 63%. Al Sayed A et al¹⁶ had also observed the frequency of dyslipidemia in patients having subclinical hypothyroidism was 67%. A study conducted in Nepal found an association between

hypothyroidism and dyslipidemia, hypercholesterolemia was found in 48.4%, hypertriglyceridemia was seen in 32.3% of hypothyroid patients.³ In a study conducted in Japan it was noted that, among hypothyroid patients, females of age more than 55 years 40.3% had high levels of low density lipoprotein cholesterol (LDL-C), which was much higher than the females of age less than 55 years (17.8%) and male patients (26.5%).¹¹ Results of the study showed that levels of triglycerides were high in SH.² Result of a study conducted in China showed that the prevalence of dyslipidemia among SH patients was higher (34.31%) than euthyroid patients (31.18%).¹² Result of a study conducted in India showed that the prevalence of dyslipidemia in SH is 65.06%.¹³ Lipoprotein lipase activity is also affected by thyroid hormone and thus affecting the hydrolysis of triglycerides into very-low, density lipoprotein (VLDL) and chylomicrons into fatty acids and glycerol.^{6,14}

CONCLUSION

The study has demonstrated and has further proved that hypothyroidism also causes dyslipidemia. Thus, it may be a good practice to screen patients with hypothyroidism for evidence of metabolic syndrome and in preventing various other complications. The screening and treatment for SH should be done to prevent its adverse effects on lipid metabolism. Thyroid hormones regulate the expression of enzymes involved in all steps of lipid metabolism leading to the development of qualitative and quantitative changes of lipids, in thyroid disease. Dyslipidemia coexists with other metabolic abnormalities, including, hypertension, insulin resistance, and oxidative stress, all of them being risk factors for other diseases. In addition, dyslipidemia induces insulin resistance and oxidative stress, via a vicious cycle. However, more studies need to be done, especially prospective, to elucidate the real significance of dyslipidemia or other metabolic changes in clinical and, even more, in subclinical hypothyroidism.

Author's Contribution:

Concept & Design of Study: Alia Banori
 Drafting: Muhammad Arshad
 Data Analysis: Shah Zeb
 Revisiting Critically: Alia Banori, Muhammad Arshad
 Final Approval of version: Alia Banori

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Success of Perfluoro Propane Gas (C_3F_8) Injection in Resolution of Vitreomacular Traction in Older Adults

C_3F_8 Injection in
Resolution of
Vitreomacular
Traction in Older
Adults

Ali Zain-ul-Abidin, Shahid Mahmood Dayal and Hasnain Mohammad Buksh

ABSTRACT

Objective: To assess the success of single injection of C_3F_8 in treatment of vitreomacular traction in adult patients.

Study Design: Quasi experimental trial

Place and Duration of Study: This study was conducted at the Department of Ophthalmology, Allama Iqbal Memorial Teaching Hospital, Sialkot from June 2017 to December 2017.

Materials and Methods: Eighteen eyes of 18 patients, of either gender with symptomatic VMT (width: 50-1500 μ m) due to idiopathic cause were included. Diabetic patients or patients with traction causing macular hole were not included. Spectral domain OCT was used to diagnose and finalize the cases. The patients were prepared and after proper aseptic measures were taken and injected with 0.3 ml of pure C_3F_8 gas intravitreally instead of doing parsplanavitrectomy (PPV). The patients were observed for the release of traction 3 months after injection. Resolution of traction was observed on OCT on every monthly visit. Success was noted in terms of resolution of VMT and patients were also evaluated for any sort of complications.

Results: The mean age of patients was 59.72 $\pm$ 2.42 years. There were 10 males and 8 females presented with VMT. Mean VMT was 746.78 $\pm$ 381.86 μ m. Out of 18 eyes, in 10 (55.5%) eyes complete resolution of VMT was achieved within one month after a single injection. Out of 8 remaining, 4 (50%) had resolution after 3 months without any further injection. However, in 4 (50%) patients, VMT could not be resolved and PPV was done to release the VMT. No complication was observed with C_3F_8 Gas injection in any patient.

Conclusion: Intravitreal perfluoro propane gas (C_3F_8) injection is an effective and safe method to release VMT in adults and single dose of C_3F_8 has a success rate of 77.8%.

Key Words: Intravitreal perfluoro propane gas injection, Vitreomacular traction, Parsplanavitrectomy, Intravitreal injection, C_3F_8 gas

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INTRODUCTION

Posterior vitreous detachment is a common phenomenon frequently related with aging of ocular structures. The presence of persistent vitreomacular adhesions exerting tractional forces vitreomacular traction (VMT) may be associated with the development of macular hole.¹ Vitreomacular traction was assumed to be an uncommon entity and not associated with other macular disorders.^{2,3} Vitreomacular traction syndrome is implicated in the pathophysiology of a number of macular disorders, translating into a variety of anatomical and functional

consequences underscoring the complexity of the condition. These macular changes are closely related to the VMT configuration and have led to proposing classification of this syndrome based on OCT findings. The size and severity of the remaining vitreomacular attachment may define the specific maculopathy. Focal VMT usually leads to macular hole formation, tractional cystoid macular edema and foveal retinal detachment, while broad VMT is associated with epiretinal membranes, diffuse retinal thickening and impaired foveal depression recovery.^{2,4,5}

The prevalence of isolated VMT syndrome is reported to be 22.5 per 100,000 populations. The annual incidence of isolated VMT syndrome is 0.6 per 100,000 populations. The prevalence and incidence of VMT associated with diabetic retinopathy, diabetic macular edema, age-related macular degeneration, and other macular diseases (concurrent VMT) is much higher. Overall, about 1.5% of the population is estimated to have eye diseases caused by or associated with VMA. The incidence of VMA diagnoses is expected to increase with widespread use of OCT and availability of pharmacologic therapies.⁶

Optical coherence tomography (OCT) has allowed better understanding and visualization of the

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vitreomacular interface. Vitreomacular adhesion and traction (VMT) are two of the many entities along the spectrum during the course of an incomplete posterior vitreous detachment, also referred to as anomalous posterior vitreous detachment.⁷

In recent years, surgical strategies in the treatment of retinal detachment have changed substantially, and intraocular surgical techniques are employed more and more. Further, the range of indications for vitreoretinal operations has widened considerably.⁸ Office-based intravitreal injection of C3F8 offers an inexpensive and effective treatment for VMT.⁹

Previous studies, investigating the release rate of VMT using intravitreal perfluoropropane (C3F8) gas showed very promising results.⁹⁻¹¹ So we planned to conduct this study to get evidence regarding the effect of a single intravitreal C3F8 gas injection with patients of VMT. In our study we planned to inject C3F8 gas injection to select 18 patients of isolated idiopathic VMT. Our main focus in the study was on the ability of the gas to separate the traction and prevent the patient from going towards the invasive parsplanavitrectomy (PPV) procedure.

MATERIALS AND METHODS

This quasi experimental trial was carried out at Department of Ophthalmology, Allama Iqbal Memorial Teaching Hospital Sialkot from 1st June 2017 to 31st December 2017. Eighteen eyes of 18 patients, or either gender age 55-65 years with symptomatic VMT (width: 50-1500 μ m) due to idiopathic cause were included. Diabetic patients or patients with traction causing macular hole (>1500 μ m), bilateral cases were excluded. Patients who presented with blurred vision or distorted images were underwent spectral domain OCT, which was used to diagnose VMT. Preoperative OCT pictures were taken afterwards they were shifted in the theatre and proper aseptic measures were taken and were injected with 0.3 ml of pure C₃F₈. The patients were prepared and after proper aseptic measures were taken and intravitreal injected with 0.3 ml of pure C₃F₈ gas. The patients were draped and 4 mm from the limbus in cases of phakic eyes and 3.5 mm pseudophakic eyes the needle was placed with gas and the needle was taken out and patients were given topical antibiotics afterwards. After injecting gas the patients were also given topical pressure lowering drugs. Special emphasis was given to prevent any infection or complication during the injection. The patients were sent home on the very same day. They were recalled and examined every month for 3 months. The patients were observed for the release of traction 3 months after injection. Resolution of traction was observed on OCT on every monthly visit. Success was noted in terms of complete resolution of VMT and patients were also evaluated for any sort of complications. Quantitative variables like age and VMT size. Qualitative variables like gender, symptoms,

success and complications were presented as frequency and percentage. Data was stratified for age, gender, VMT size and symptoms. Post-stratification, chi-square was applied to compare the success in stratified groups with p-value $\leq$ 0.05 taken as significant.

RESULTS

The mean age of patients was 59.72 $\pm$ 2.42 years. There were 10 males and 8 females presented with VMT. In the sample, 7 (38.9%) patients presented with complaint of blurred vision while 11 (61.1%) had distorted images. Mean VMT was 746.78 $\pm$ 381.86 μ m. There were 5 (27.8%) cases with VMT width 50-500 μ m, 8 (44.4%) had VMT width 501-1000 μ m and 5 (27.6%) had VMT width 1001-1500 μ m (Table 1). Out of 18 cases, in 14 (77.8%) cases, success was achieved with single C3F8 injection (Fig. 1). In 10 (55.5%) eyes complete resolution of VMT was achieved within one month after one injection. Among remaining 8 cases, 4 (50%) achieved complete resolution within 3 months without any further injection. However, in 4 (50%) patients, VMT could not be resolved and PPV was done to release the VMT. No complication was observed with C3F8 Gas injection in any patient (Table 2). Data was stratified for age, gender, symptoms and VMT width. In patients aged 55-60 years, success was achieved in 9 (90%) cases while in patients aged 61-65 years, success was achieved in 5 (62.5%), but the difference was insignificant (p>0.05). In males, success was achieved in 8 (80%) cases while in females, success was achieved in 6 (75%) and the difference was insignificant (p>0.05).

Table No.1: Baseline characteristics of patients (n=18)

Age (years)	59.72 $\pm$ 2.42
Sex	
Male	10 (55.6%)
Female	8 (44.4%)
Symptoms	
Blurred vision	7 (38.9%)
Distorted images	11 (61.1%)
VMT size (μ m)	746.78 $\pm$ 381.86
VMT width 50-500 μ m	5 (27.8%)
VMT width 501-1000 μ m	8 (44.4%)
VMT width 1001-1500 μ m	5 (27.8%)

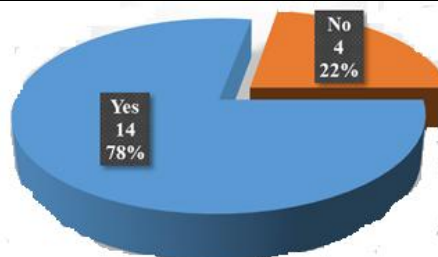


Figure No.1: Distribution of success of C3F8 injection

In patients with blurred vision, success was achieved in 6 (85.7%) cases while in patients with distorted vision, success was achieved in 8 (72.7%) and the difference was insignificant ($p>0.05$). In patients with VMT width 50-500 μ m, success was achieved in 5 (100%) cases, in patients with VMT width 501-1000 μ m, success was achieved in 8 (100%) while in patients with VMT width 1001-1500 μ m, success was achieved in 1 (20%) case only and the difference was significant ($p<0.05$) (Table 3).

Table No.2: Outcome of C3F8 injection

Resolution in first month	10 (55.5%)
Resolution in 3 months	4 (22.2%)
Failure (no resolution)	4 (22.2%)
PPV (in failure cases)	4 (22.2%)
Complication	0 (0.0%)

Table No.3: Comparison of VMT release in age, gender, VMT width and symptoms strata

Variable	VMT release		Total	p value
	Yes (14 cases)	No (4 cases)		
Age: 55-60 years	9 (90%)	1 (10%)	10	0.163
Age: 61-65 years	5 (62.5%)	3 (37.5%)	8	
Male	8 (80%)	2 (20%)	10	0.800
Female	6 (75%)	2 (25%)	8	
Blurred vision	6 (85.7%)	1 (14.3%)	7	0.518
Distorted image	8 (72.7%)	3 (27.3%)	11	
VMT width 50-500 μ m	5 (100%)	0 (0.0%)	5	0.001
VMT width 501-1000 μ m	8 (100%)	0 (0.0%)	8	
VMT width 1001-1500 μ m	1 (20%)	4 (80%)	5	

DISCUSSION

With age, the vitreous gel undergoes liquefaction forming pockets of fluid within the vitreous which leads to a contraction or condensation of the vitreous. With loss of vitreous volume, there is a tractional pull exerted at sites of vitreoretinal and vitreopapillary attachments by means of the condensing dense vitreous cortex. At the same time, there is weakening of these attachments between the vitreous and the internal limiting membrane and it is proposed that detachment of the posterior hyaloid proceeds in the following sequence: (i) Perifoveal region (possibly, temporal followed by nasal), (ii) Superior and inferior vascular arcades, (iii) Fovea, (v) Mid-peripheral retina or (vi) Optic disc.^{1,12} Approximately two-thirds of patients with macular hole are women, and the disease is unilateral in 80% of cases. An increase in serum fibrinogen level has been reported as a risk factor for macular hole, whereas the use of estrogen replacement therapy in women decreases the risk.^{13,14} In subjects with myopia, the prevalence of macular hole may reach 6%.¹⁵ In our study, the mean age of patients was 59.72 $\pm$ 2.42 years.

There were 10 males and 8 females presented with VMT. In the sample, 7 (38.9%) patients presented with complaint of blurred vision while 11 (61.1%) had distorted images. Mean VMT was 746.78 $\pm$ 381.86 μ m. There were 5 (27.8%) cases with VMT width 50-500 μ m, 8 (44.4%) had VMT width 501-1000 μ m and 5 (27.6%) had VMT width 1001-1500 μ m.

In our study, out of 18 cases, in 14 (77.8%) cases, success was achieved with single C3F8 injection. In 10 (55.5%) eyes complete resolution of VMT was achieved within one month after one injection. Among remaining 8 cases, 4 (50%) achieved complete resolution within 3 months without any further injection. However, in 4 (50%) patients, VMT could not be resolved and PPV was done to release the VMT. No complication was observed with C3F8 Gas injection in any patient.

Haas et al¹⁶ found that six of seven eyes (85.7%) had release of VMT during the entire study duration: three within 1 month of injection and the other three within 6 months. They concluded that Intravitreal C3F8 gas injection is an inexpensive and promising minimally invasive option for the treatment of symptomatic and persistent VMT. Further larger studies, especially comparing C3F8 gas injection with other treatment options, are needed.

The Ocriplasmin for Treatment for Symptomatic Vitreomacular Adhesion Including Macular Hole (OASIS) study reported even higher rates: 41.7% of patients in the ocriplasmin group had VMT release on day 28.¹⁷ Sharma et al. found the resolution of VMT to be as high as 50% in their sample. All these studies only reported on the results of VMT resolution 28 days after the intravitreal injection.¹⁸

Recently, Claus et al¹⁹ reported a high VMT release rate by intravitreal C₂F₆ or SF₆ injection, with 1 out of 20 (5%) eyes developed full-thickness macular hole subsequently. They concluded that the type of gas used has only a minor influence on the result. Steinle et al⁹ found that overall, VMT release occurred in 25 of 30 eyes by the final follow-up visit (83% final release rate). So office-based intravitreal injection of C3F8 offers an inexpensive and effective treatment for VMT.

We stratified the data for age, gender, symptoms and VMT width. In patients aged 55-60 years, success was achieved in 9 (90%) cases while in patients aged 61-65 years, success was achieved in 5 (62.5%), but the difference was insignificant ($p>0.05$). In males, success was achieved in 8 (80%) cases while in females, success was achieved in 6 (75%) and the difference was insignificant ($p>0.05$). In patients with blurred vision, success was achieved in 6 (85.7%) cases while in patients with distorted vision, success was achieved in 8 (72.7%) and the difference was insignificant ($p>0.05$). In patients with VMT width 50-500 μ m, success was achieved in 5 (100%) cases, in patients with VMT width 501-1000 μ m, success was achieved in 8 (100%) while in patients with VMT width 1001-1500 μ m, success was achieved in 1 (20%) case only and the difference was significant ($p<0.05$). This showed that C3F8 is highly effective for small VMT width area, while for large areas, PPV would be done. But number

of unnecessary surgeries can be prevented and a single dose of C3F8 can be beneficial in VMT release.

Pneumatic vitrolysis was for the very first time given in 2014 and afterwards continuously tried in cases of VMT but during those times it was given with ocriplasmin as a preoperative tool.¹⁹ After the injection VMT was released in 80% of the patients.^{9,20} Overall safety of the procedure is very much in the favour of giving the patient the chance of intravitreal gas injection before vitrectomy. None of any case so far is reported with infection due to gas injection. Release of VMT with gas injection should always be considered in idiopathic VMT.

CONCLUSION

Intravitreal perfluoro propane Gas (C3F8) injection is an effective and safe method to release VMT in adults and single dose of C3F8 has a success rate of 77.8%. Thus we have got the evidence which favors the C3F8 injection for release of VMT in focal type of VMT (Width of attachment $\leq 1500 \mu\text{m}$). So in future, C3F8 will be considered as first line management protocol for release of VMT.

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Correlation of Serum Sodium with Severity of Hepatic Encephalopathy

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Serum Sodium with
Severity of Hep.
Encephalopathy

ABSTRACT

Objective: To study the correlation of serum sodium with severity of hepatic encephalopathy HE.

Study Design: Cross sectional (Correlational) study.

Place and Duration of Study: This study was conducted at Naseer Teaching Hospital Peshawar from October 2017 to September 2018.

Materials and Methods: This study was conducted on 408 patients who were observed by using - 0.1411 of correlation coefficient between serum sodium (S.Na) and HE 95% confidence level and 80% power of test. More over non probability consecutive sampling was used for sample collection. The patients were collected from medical ward of NTH. After taking informed consent, clinical data were collected on a proforma designed for study. S.Na was evaluated in all cases of both groups and results were tabulated.

Results: In this study mean age was 65 years with SD $\pm$ 0.315. Sixty-two percent patients were male and 38% patients were female. Mean S.Na (S.Na) level was 123 meq/L with SD $\pm$ 0.21. Five percent patients had severity of grade I, 39% patients had severity of grade II, 48% patients had severity of grade III and 8% patients had severity of grade IV. Correlation of severity of HE with S.Na level was analyzed as all the 20 patients with severity of grade I had S.Na level ranged 131 -133 meq/L. All the 159 patients with severity of grade II had S.Na level ranged 126-130 meq/L. In 196 patients with severity of grade III, 45 patients had S.Na level ranged 126-130 meq/L while 151 patients had S.Na level ranged 120-125 meq/L whereas all the 33 patients with severity of grade V had S.Na level ranged 120-125 meq/L.

Conclusion: Hyponatremia was a common feature in patients with cirrhosis and its severity increased with the severity of liver disease. The existence of S.Na concentration <135 mmol/L was associated with greater frequency of HE. It was also noticed that more severe the hyponatremia, greater will be the grade of HE.

Key Words: Hepatic encephalopathy, frequency, cirrhosis, spontaneous bacterial peritonitis

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INTRODUCTION

Cirrhosis is a serious and irreversible disease. It is a major cause of mortality and morbidity worldwide. Cirrhosis develops in about 10-20 years. The most common cause in Pakistan is viral hepatitis as compared to West where alcohol is more common.¹ Hepatic encephalopathy (HE) is neuropsychiatric syndrome for which symptoms, manifested on a continuum, is deterioration in mental status, with psychomotor dysfunction, impaired memory, increase reaction time, poor concentration, disorientation, and in

severe form coma² and may develop at an annual rate of 8% in cirrhotic patients in Far Eastern studies³. Cirrhosis-related expenses impact the family unit's daily functioning and medical adherence. A multidisciplinary approach to address this burden is required.⁴ The clinical diagnosis is based on two types of symptoms: impaired mental status⁵ and impaired neuromotor function.² Fluctuation in serum sodium level is a frequent complication of advanced cirrhosis.⁶ Hyponatremia is a common finding in patients with decompensated cirrhosis due to an abnormal regulation of body fluid homeostasis.⁷ Literature review suggested an association between S.Na concentration and hepatic encephalopathy that S.Na and serum ammonia concentrations have been the major determining factors for abnormal electroencephalographic findings in HE patients and S.Na acts as an independent risk factor for HE.^{6,8} It has also been observed that low S.Na levels are a very common finding in patients with hepatorenal syndrome⁹. The present study is designed to determine the correlation between S.Na level and severity of hepatic encephalopathy. As mentioned above, the S.Na level is a strong predictor of severity of hepatic encephalopathy and also the literature suggested a bit variation in the correlation coefficient between S.Na level and severity of HE. This study will provide us

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with local statistics about the correlation of sodium level and HE.

MATERIALS AND METHODS

This study was conducted at Naseer Teaching Hospital Peshawar. Duration of the study was 1 year and the study design was cross sectional (Correlation) study in which a total of 408 patients were observed by using - 0.1411 of correlation coefficient between S.Na and HE 95% confidence level and 80% power of test. More over non probability consecutive sampling was used for sample collection. Patients presenting within 24hr of onset of HE aged 18 years and above were included while Patients with concomitant chronic renal failure, patients with acute fulminant hepatitis, Patients having spontaneous bacterial peritonitis on admission were excluded. The above mentioned conditions act as confounders and had cause bias in the study results if not excluded. Data collected was entered in SPSS 16. Results were presented as tables and graphs.

RESULTS

In this study 408 patients were observed in which 126(31%) patients were in age ranged 40-50 years, 135(33%) patients were in age ranged 51-60 years and 147(36%) patients were in age ranged 61-70 years. Mean age was 65 years with $SD \pm 0.315$. Two hundred fifty-three (62%) patients were male while 155(38%) patients were female. One hundred eighty-four (45%) patients had S.Na level ranged 120-125 meq/L, 204(50%) patients had S.Na level ranged 126-130 meq/L and 20(5%) patients had S.Na level ranged 131-133 meq/L.

Table No.1: Age Distribution (n=408)

Age	Frequency	Percentage
40-50 Years	125	31%
51-60 Years	135	33%
61-70 Years	147	36%
Total	408	100%

Table No.2: Gender Distribution (n=408)

Gender	Frequency	Percentage
Male	253	62%
Female	155	38%
Total	408	100%

Table No.3: S.Na Level (n=408)

S.Na Level (MEQ/L)	Frequency	Percentage
120-125	184	45%
126-130	204	50%
131-133	20	5%
Total	408	100%

Mean S.Na level was 123 with $SD \pm 0.21$

Table No.4: Severity of Hepatic Encephalopathy (n=408)

Severity of Hepatic Encephalopathy	Frequency	Percentage
Grade I	20	5%
Grade II	159	39%
Grade III	196	48%
Grade IV	33	8%
Total	408	100%

Table No.5: Correlation of Severity of Hepatic Encephalopathy With S.Na Level (n=408)

		S.Na Level			Total
		120-125	126-130	131-133	
Severity of Hepatic Encephalopathy	Grade I	0	0	20	20
	Grade II	0	159	0	159
	Grade III	151	45	0	196
	Grade IV	33	0	0	33
	Total	184	204	20	408

Spearman's rank correlation coefficient was 2.28 P value was 0.0001

Mean S.Na level was 123 meq/L with $SD \pm 0.21$. Severity of hepatic encephalopathy was measured in term of grades and was analyzed as 20(5%) patients had severity of grade I, 159(39%) patients had severity of grade II, 196(48%) patients had severity of grade III and 33(8%) patients had severity of grade IV. Correlation of severity of hepatic encephalopathy with S.Na level was analyzed as all the 20 patients with severity of grade I had S.Na level ranged 131-133 meq/L. All the 159 patients with severity of grade II had S.Na level ranged 126-130 meq/L. In 196 patients with severity of grade III, 45 patients had S.Na level ranged 126-130 meq/L while 151 patients had S.Na level ranged 120-125 meq/L whereas all the 33 patients with severity of grade IV had S.Na level ranged 120-125.

DISCUSSION

In our study correlation of severity of hepatic encephalopathy with S.Na level was analyzed as all the 20 patients with severity of grade I had S.Na level ranged 131-133 meq/L. All the 159 patients with severity of grade II had S.Na level ranged 126-130 meq/L. In 196 patients with severity of grade III, 45 patients had S.Na level ranged 126-130 meq/L while 151 patients had S.Na level ranged 120-125 meq/L whereas all the 33 patients with severity of grade IV had S.Na level ranged 120-125 meq/L. Spearman's rank correlation coefficient was — 0.28. Similar results were found in a study done by Sanyal A et al¹⁰ as he reported correlation between S.Na level and severity of HE is -0.5830. Montono LA et al¹¹ had reported

correlation of S.Na level and severity of HE as -0.14. S.Na predicts prognosis in cirrhosis and may improve the prognostic accuracy of the model for end stage liver disease (MELD) score, but the available information is limited¹². Saad M et al¹³ had reported that patients with low S.Na tend to have more severe ascites ($p = 0.001$). Hepatic encephalopathy was more frequent in patients with S.Na $<130\text{meq/l}$ ($p = 0.001$). In another study conducted by Cardenas et al¹⁴ shows that more than one half (57.9%) of patients had values of S.Na concentration below the normal range ($<135\text{meq/l}$) and 30.7% had values $<130\text{meq/l}$. The frequency of S.Na $<130\text{mmol/L}$ in these patients is in accordance with a study by Borroni et al.¹⁵ who reported hyponatremia in 30% of cases. In a Pakistani study it was found to be 26.7%.¹³ The prevalence of HE was greater (34.15%) as compared to other national and international studies. The patients with S.Na $<130\text{meq/l}$ had a significantly greater frequency (64%) of HE. The relationship between hepatic encephalopathy and serum levels may be explained on the basis of more severe liver failure among patients with S.Na $<130\text{meq/l}$, and the possibility that the two events may be pathophysiological linked¹⁶. Low S.Na levels in patients with cirrhosis are associated with a remarkable reduction in the cerebral concentration of organic osmolytes that probably reflect compensatory osmoregulatory mechanisms against cell swelling.¹⁷⁻²⁰ A major advance in our ability to treat hyponatremia is the introduction and approval of aquaretics (vaptans) which are vasopressin V2-receptor antagonists.²¹ In a study with 156 patients hospitalized with liver cirrhosis, the prevalence of hyponatremia, based on a S.Na concentration $\leq 130\text{mmol/L}$, was 29.8%, and hyponatremia was significantly correlated with infection and ascities²².

CONCLUSION

Hyponatremia was a common feature in patients with cirrhosis and its severity increased with the severity of liver disease. The existence of S.Na concentration $<135\text{mmol/L}$ was associated with greater frequency of hepatic encephalopathy. It was also noticed that more severe the hyponatremia, greater will be the grade of hepatic encephalopathy. Close monitoring of S.Na concentration should be performed in patients with cirrhosis in order to prevent the rapid development of cirrhosis related complications.

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Pattern of Acinetobacter Species Isolated from Critically ill Patients of a Tertiary Care Hospital

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ABSTRACT

Objective: to isolate Acinetobacter species and to evaluate its antibiotic susceptibility pattern in all types of clinical specimens of critically ill patients of Jinnah Hospital, Lahore.

Study Design: Cross sectional study

Place and Duration of Study: This study was conducted at the Pathology Department, Allama Iqbal Medical College, Lahore from 1st July 2015 to 31st December 2015.

Materials and Methods: One hundred clinical specimens obtained from the critically ill patients admitted in Jinnah Hospital, Lahore, were cultured using standard microbiological techniques and antimicrobial susceptibility pattern was evaluated using modified Kirby Bauer disc diffusion method following CLSI guidelines 2015.

Results: The isolation rate of Acinetobacter baumannii was high as compared to the other species. Most of them were identified from the blood samples followed by the tracheal secretions and pus samples. The isolation rate of overall Acinetobacter species was high in ICU's and surgical wards. Antimicrobial susceptibility pattern revealed resistance rate of Acinetobacter species as co-trimoxazole 96(96%), gentamicin 82(82%) and ciprofloxacin 84(84%). Almost all of the isolates were susceptible to tigecycline and colistin.

Conclusion: Acinetobacter species were resistant to most of the commonly used antibiotics. Only tigecycline has good susceptibility i.e 72% and colistin 100% susceptible to the Acinetobacter isolates from intensive care units.

Key Words: Acinetobacter baumannii, nosocomial pathogen, colistin, tigecycline

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INTRODUCTION

Acinetobacter species is one of the most common cause of nosocomial infections. It was originally given the name as Acinetobacter after the baumann's et al in 1968. Acinetobacter species is gram negative and aerobic coccobacilli¹, non-lactose fermenting, encapsulated gram negative opportunistic pathogen. Acinetobacter species is not fastidious and is pleomorphic.²

Acinetobacter species readily colonizes skin, oropharyngeal secretions and respiratory tract parts.³ There are almost 35 known species of Acinetobacter that has been identified so far.⁴

Multidrug resistant Acinetobacter species has been involved in meningitides, bacteremia, nosocomial pneumonia, skin and soft tissue infections, urinary tract infections and the infections at the sites of trauma and surgery etc.⁵ Acinetobacter baumannii is mostly found on the surface of the medical devices. Acinetobacter species are mostly frequently found in the ICU's of the hospital.⁶ Another unique property of the mutant Acinetobacter strains BD413trpe27 has been observed that is naturally transformable tryptophan auxotrophic to the wild type phenotype.⁷ Acinetobacter species resist the sterilization and disinfection processes because of its ability to form biofilm which along with the resistance towards the disinfection also plays an important role in its attachment to the medical devices.

A recent study also revealed that the colonies of the Acinetobacter species can persist in their mucoid form for at least 6 days increasing its pathogenicity. A recent study conducted by Grace et al in 2016 shows that mutations in two of the genes of the two component system (TCS's) namely AdeR and AdeS which are involved in the formation of adeA, adeB, adeC (RND family) which causes the efflux of the antibiotics out of the cell hence making it multidrug resistance. Acinetobacter species has the ability to produce six different types of QS molecules.⁸ Microbial resistance is

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a natural biological response of the organism towards the antibiotics, heat, environment, food and acquired. Antimicrobial resistance mechanisms include antimicrobial inactivation by the enzymes, reduced access to the bacterial targets and mutations that changes the targets or cellular functions.⁹

Acinetobacter species produces different Ambler classes of enzymes that act as carbapenemases. Ambler class A, extended spectrum β – lactamases (ESBL), includes PER 1, PER 2, VEB 1, TEM 1, TEM 2, SHV, CTX-M.¹⁰ Ambler class B, Metallo β lactamases (MBL) include IMP, VIM, SIM. Ambler class D is the main cause of carbapenem resistance in *Acinetobacter* species. It is also known as OXA carbapenemases. These enzymes acts in the periplasm and convert their monomeric (less active) form into dimeric (more active) form and producing greater amount of carbapenemase activity.¹¹

Acinetobacter species with these altered proteins have 0.5% less permeability as compared to other enterobacteriaceae which plays an important role in the prolonged survival as nosocomial pathogen.¹²

Acinetobacter species produces plasmids or chromosomal mediated aminoglycosides mediated enzymes (AME's) that causes the modifications of aminoglycosides. *Acinetobacter* species causes the over production of the AdeABC efflux pump which causes the efflux of tetracyclines out of the bacterial cell.¹³

Acinetobacter species has the great ability to tolerate the harsh environment, dryness, PH and temperature basically DNA damage and cellular damaging by the production of RecA gene.¹⁴

MATERIALS AND METHODS

This study was carried out in Pathology Department, Allama Iqbal Medical College, Lahore. 100 isolates were included from different clinical specimens of critically ill patients that were admitted in Jinnah Hospital, Lahore. All types of samples were included in the study including urine, blood, pus, pus swabs, tracheal secretions, sputum, CVP tip and body fluids.

The preliminary identification of bacteria was done by standard microbiological procedures including colonial morphology, gram staining, catalase test, oxidase test. *Acinetobacter* isolates were confirmed by using API 20NE (Biomérieux, France), according to the manufacturer's instructions.

Antimicrobial susceptibility of these isolates was performed by Modified Kirby Bauer disc diffusion method using Mueller-Hinton agar (Oxoid UK), bacterial suspension equal to 0.5 McFarland turbidity standard and the plates were lawned and incubated at 35°C for 24 hours. Zone sizes were interpreted according to Clinical Laboratory Standards Institute (CLSI) 2015 guidelines. *Acinetobacter baumannii* ATCC 19606 was used as quality control strain.¹⁵

RESULTS

A total of total 100 *Acinetobacter* isolates from clinical samples of all types were included. All the culture positive isolates showed characteristic non fermenting colonies on MacConkey, Gram staining of all the isolates showed typical gram negative coccobacillary morphology. All the isolates were catalase positive and oxidase negative. API 20NE was used for identification of *A. baumannii* from the other species.

Out of total 100 isolates 25 were isolated from the tracheal secretions, 19 from the blood specimens, 22 from the wound/swabs, 6 from the sputum samples, from the urine, 5 from the CVP line tip, 19 from the pus specimens and 1 from the wound/swabs and pus specimens.

Out of 100 isolates 73(73%) were positive for *A. baumannii* and 27(27%) were other species of *Acinetobacter*. Out of total 100 *A. baumannii*, 54(54%) were found in male and 19(19%) were in females. Total isolates found in males were 68(68%) and among females that were 32(32%).

A total of 26 isolates were from the ICU out of which 21(29%) were *A. baumannii* and 5(18.5%) were *Acinetobacter* species, 17 from the surgical wards out of which 13(18%) were *A. baumannii* and 4(15%) were *Acinetobacter* species, 10 were from orthopedic out of which 9(12.3%) were *A. baumannii* and 1(3.7%) was *Acinetobacter* species, 6 from dermatology out of which 5(7%) were *A. baumannii* and 1(3.7%) was *Acinetobacter* species, 1 from ENT ward and was *Acinetobacter* species, 7 from neurosurgery out of which 5(6.8%) were *A. baumannii* and 2(7.4%) were *Acinetobacter* species, 4 from pulmonology out of which 1(1.4%) was *A. baumannii* and 3(11.1%) were *Acinetobacter* species, 16 from the pediatric ward out of which 4(12.3%) were *A. baumannii*, 7(25.8%) were *Acinetobacter* species and 2 from the gynaecology, out of which 1(1.4%) was *A. baumannii* and 1(3.7%) was *Acinetobacter* species.

Out of total 73 isolates of *A. baumannii*, 73(100%) isolates of *Acinetobacter baumannii* were resistant to piperacillin-tazobactam, 54(74%) were resistant to cefoperazone-sulbactam, 52(71%) were resistant to amikacin, 63(86%) were resistant to gentamicin, 64(88%) were resistant to ciprofloxacin, 54(74%) were resistant to imipenem and meropenem, 67(92%) were resistant to doxycycline, 28(38%) were resistant to tigecycline, 70(96%) were resistant to co-trimoxazole and 73(100%) isolates were susceptible to colistin.

Out of total 27 isolates of *Acinetobacter* species, 26(96%) isolates of *Acinetobacter* species were resistant to Ampicillin 26(96%) to co-amoxyclove, 25(93%) were resistant to ceftriaxone, 21(78%) were resistant to piperacillin-tazobactam, 14(52%) were resistant to gentamicin, 20(74%) were resistant to ciprofloxacin, 11(44%) were resistant to tigecycline,

26(96%) were resistant to co-trimoxazole and 27(100%) isolates were susceptible to colistin.

Table No.1: Acinetobacter species distribution among different wards

Wards	A. baumannii n=73	Acinetobacter species n=27
Surgical wards	13 (18%)	3(11.1%)
Intensive care unit(ICU)	21(29%)	5(18.5%)
Critical care unit(CCU)	2(3%)	0(0%)
Dermatology	5(7%)	1(3.7%)
ENT	0 (0%)	1(3.7%)
Medical wards	7(9.5%)	3(11.1%)
Pediatric ward	9(12.3%)	7(25.9%)
Orthopedic wards	9 (12.3%)	1(3.7%)
Neurosurgery	5(6.8%)	2 (7.4%)
Gynecology Wards	1(1.4%)	1 (3.7%)
Pulmonology	1(1.4%)	3 (11.1%)



Figure No.1: Antibiotic sensitivity of Acinetobacter species on Muller Hinton Agar

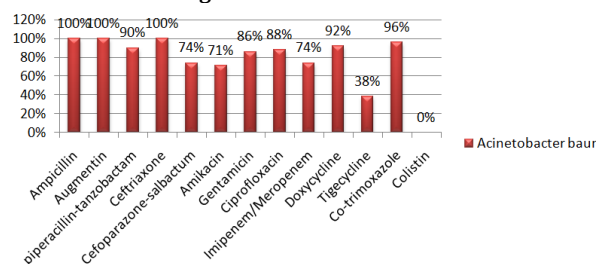


Figure No.2: Antibiotic Resistance Pattern Among Acinetobacter baumannii

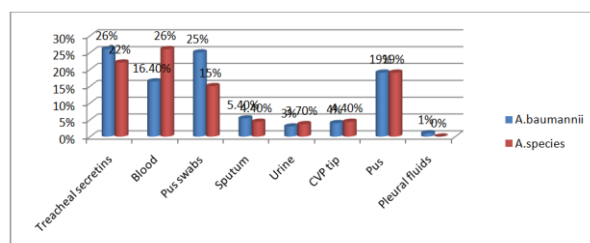


Figure No.3: Antibiotic Resistance Pattern Among Acinetobacter species

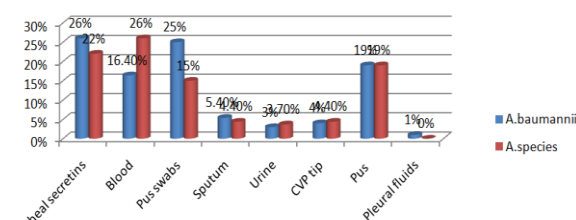


Figure No.4: Specimen wise distribution of Acinetobacter species

DISCUSSION

Acinetobacter is also known as "Iraqibacter", since 1980's uptill now it has been one of the emerging problems in the health care sectors. Many of the factors associated with the mutations and acquired resistance are making it more resistant as a superbug day by day.¹⁶ In this study 100 clinical samples of all types were included. 100% isolates of *Acinetobacter baumannii* showed resistance against ampicillin and co-amoxyclove as compared to 96% and 96% isolates of *Acinetobacter species* respectively. *Acinetobacter baumannii* and *Acinetobacter species* were 100% and 93% resistant to ceftriaxone, 86% and 70% resistant to gentamicin, 71% and 26% resistant to amikacin, 74% and 52% resistant to cefepime-salbutam, 90% and 78% resistant to piperacillin-tazobactam, 88% and 74% resistant to ciprofloxacin, 74% and 56% resistant to meropenem / imipenem, 92% and 93% resistant to doxycycline, 96% and 96% resistant to co-trimoxazole, 38% and 41% resistant to tigecycline respectively. All the species of *Acinetobacter* shows 100% susceptibility against colistin.

A local study conducted at General hospital in 2013 by Sohaila et al showed similar results. In that study 90 isolates were included and 66% *Acinetobacter baumannii* were resistant to meropenem and piperacillin-tazobactam, 50% resistant to ciprofloxacin as compared to our study in which it is 64% resistant. Out of total, 31% isolates were resistant to tetracycline but in our study it resistance is 38%, 50% resistant to gentamicin but in our study it is 86% resistant, ceftriaxone is 44% resistant but in our study it is 100% resistant. Both of the studies include all types of the clinical specimens. There is a marked increasing resistance of ceftriaxone in our study as compared to Sohaila et al.¹⁷

A study carried out in India in 2014 by Tripathi et al included 107 clinical specimens, 74% cultures were positive from the general wards while 11.96% cultures were positive from the ICU's. In that study 57% isolates of *Acinetobacter species* were resistant to imipenem while in our study it is 74%. Out of total, 55% are resistant to amikacin but in our study it is 71% resistant. *Acinetobacter species* were 100% resistant to Piperacillin-tazobactam while in our study it is 90% resistant to piperacillin-tazobactam. Due to the increase

use of piperacillin-tazobactam *Acinetobacter* is also acquiring the resistance against it.¹⁸

A study carried out in a tertiary care hospital at Dhaka by Azizun Naharet al in 2012 included 95 samples from the critically ill patients of ICU's. *Acinetobacter* species were 100% resistant against co-amoxyclove in that as well as in our study. In that study 68.4% isolates were resistant against amikacin while in our study it is 71%. In that study meropenem is 66.7% resistant against *Acinetobacter* species while in our study it is 74% resistant. Gentamicin according to that study is 100% resistant to *Acinetobacter* species while in our study it is 86% resistant. That study revealed the presence of 54.3% *Acinetobacter* species in tracheal secretions while in our study it is 25%. Our study also discloses the highest rate of presence of *Acinetobacter* species in the tracheal secretions as compared to other specimens.⁴ Another study carried out in India in 2015 by Gitanjali et al included 3298 infected samples, 111 (3.36%) were found to be *Acinetobacter* species while in our study 100 isolates of *Acinetobacter* were included. The most predominant species was *Acinetobacter calcoaceticus*-*A. baumannii* (Acb) complex i.e 72% while in our study it is 73%. High incidence of resistance was recorded for Piperacillin-tazobactam (55%) but in our study piperacillin-tazobactam was resistant to 90% of the isolates, followed by ceftriaxone (46%) and ceftazidime (46%) while in our study it is 100%. The studies supports the fact that *Acinetobacter baumannii* is the most commonly occurring nosocomial pathogen as compared to other species of *Acinetobacter*.²

CONCLUSION

Acinetobacter associated hospital acquired infection are rising with passage of time. Antimicrobial resistance is also rising among *Acinetobacter* species.

Author's Contribution:

Concept & Design of Study:	Fizza Khan
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Data Analysis:	Kokab Jabeen, Farhan Rasheed
Revisiting Critically:	Fizza Khan, Hafiz Haseeb Afsar
Final Approval of version:	Fizza Khan

Conflict of Interest: The study has no conflict of interest to declare by any author.

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Clinical and Epidemiological Aspects of Basal Cell Carcinoma in Karachi

Shaima S. Memon¹, Pushpa Vali Ram¹ and Nasimah Iqbal²

ABSTRACT

Objective: To study the clinical and epidemiological aspects of Basal Cell Carcinoma in Karachi and to compare this with western and local literature.

Study Design: A descriptive study.

Place and Duration of Study: This study was conducted at the Department of Pathology, PNS Shifa (Naval Hospital), Karachi from January 2012 to June 2015.

Materials and Methods: All forty cases of Basal Cell Carcinoma diagnosed at PNS Shifa during the study period were included in the study. Skin biopsies were received at the Histopathology Laboratory. Age, gender, occupation, ethnic group, clinical presentation and history of any predisposing factors were recorded on a specially prepared proforma. Gross examination was performed; representative sections taken and tissues submitted for further processing. Microscopic examination was performed thereafter.

Results: Elderly males were most commonly affected. Punjabis were the commonest ethnic group affected (42.5%). The commonest site was the face (72.3%). Two thirds of the patients had professions involving prolonged sun exposure. Most of the patients had solitary lesions (92.5%) with only three patients (7.5%) having multiple lesions. One patient had a positive family history of basal cell carcinoma (mother) and two patients had predisposing skin conditions.

Conclusion: Basal Cell Carcinoma in Karachi is not uncommon. The findings of our study are in concurrence with local and western studies. However further studies need to be done to examine various clinical and epidemiological parameters in different parts of Pakistan.

Key Words: Basal cell carcinoma, clinical, epidemiological, Karachi

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INTRODUCTION

Basal cell carcinoma (BCC) is a malignant tumour of skin which arises from basal cells of the surface epidermis and its appendages¹. The nomenclature of this lesion has been the subject of great controversy as evidenced by the fact that it is known by various names including basal cell epithelioma, basalioma, rodent ulcer, Jacobi's ulcer, rodent carcinoma, adnexal carcinoma and non-Malpighian epithelioma. Some authors are reluctant to label it as a carcinoma because of absence of cellular atypia and the fact that it almost never metastasises. However, by general consensus, the most preferred term is basal cell carcinoma in

recognition of its origin, locally invasive nature and its ability to metastasise (although extremely rare). It is the commonest malignant skin tumour affecting white races.^{2,3} Traditionally it has been uncommon in blacks and Asians, but the incidence is increasing. Since there is very little in local literature about the subject, a need was felt to study various aspects of this disease further. The purpose of this study was to study the clinical and epidemiological spectrum of BCC in Karachi and to compare this with western and local literature.

MATERIALS AND METHODS

This was a retrospective as well as prospective study of cases of BCC at PNS Shifa (Naval Hospital), Karachi over a three and a half year period from January 2012 to June 2015.

The study covered epidemiological aspects like age, sex, occupation and ethnicity; as well as clinical aspects like nature, site and duration of lesion, and whether or not there were any predisposing factors or family history.

Forty cases of BCC were diagnosed at PNS Shifa, Karachi during the study period and all of these were included. Skin biopsies of known and suspected cases of BCC were taken by the dermatologist or surgeon, immediately placed in 10% formal saline and dispatched to the Department of Pathology, PNS Shifa.

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At the laboratory the sample went through routine examination and processing. After microscopy, all data was recorded and then analysed using SPSS 20 software. Pubmed was used for literature search.

RESULTS

Out of 40 patients studied, 26 (65%) were male (Fig 1). The commonest age group affected was the 60-69 year age group with 40% of patients falling in this bracket (Fig 2). The youngest being 30 and the eldest 75 years old.

Ethnic origin of 8 of the patients was unknown. Out of the remaining 32 patients, the majority were Punjabi (17), followed by Pathans (8), Sindhi (4), Kashmiri (2) and Balochi(1).(Fig 3)

All 14 of the female patients were housewives. Eight patients' occupations were unknown. Four patients were farmers and 4 were labourers. Two patients were soldiers in the Pakistan Army. The remaining 8 patients had a variety of professions among them (Table I).

The duration of the disease was unknown in 8 of the cases. Of the remaining 32 cases, 16 patients gave a history of >5 years duration. Four patients had a relatively short duration of <1 year. Six patients gave a 1-2 year history and 6 patients gave a 2-5 year history. Thirty seven of the patients had solitary lesions with 3 patients having multiple lesions. Out of the 3 patients with multiple lesions, 2 patients had 2 lesions each, and 1 patient (an albino) had 6 lesions. This gave a total of 47 lesions studied. All the lesions were painless. Three lesions arose in nevi and scars (Table 2).

Thirty four (72,3%) of the lesions were situated on the face. Four lesions were on the back, 2 on the ear and 2 retroaural in location. The remaining 5 lesions occurred on the chest wall, scalp, axilla, vulva and dorsum of the hand (Table 3).

Three out of 40 patients studied had predisposing factors. One patient who had 2 lesions on his forehead had epidermodysplasia verruciformis and bowenoid dysplasia elsewhere on his face. Another patient who had 6 lesions on his nose, ear, retroaural keratosis lesions elsewhere on his face and arms. A 3rd patient, a 35 year old male, had a family history. His mother also had BCC and was included in this study.

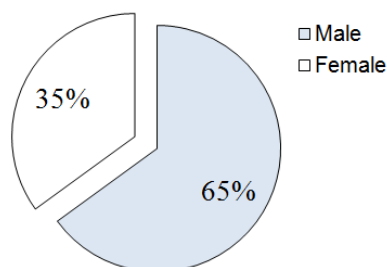


Figure No.1: Sex Distribution of BCC

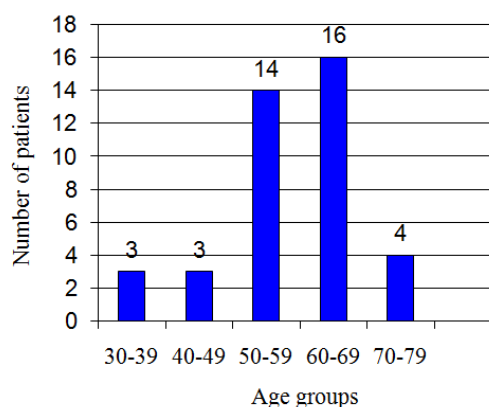


Figure No.2: Age Group Distribution of BCC (n=40)

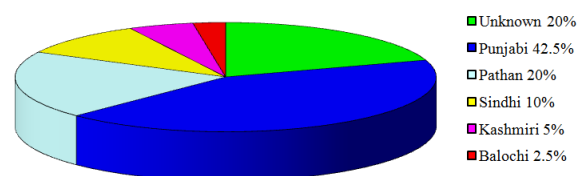


Figure No.3: Ethnic Group Distribution of BCC

Table No.I: Occupational Distribution of BCC n=40

Occupation	Number of Patients	Percentage
Housewife	14	35%
Unknown	8	20%
Farmer	4	10%
Labourer	4	10%
Sepoy	2	5%
Carpenter	1	2.5%
Pipefitter	1	2.5%
Driver	1	2.5%
Ex-pilot	1	2.5%
Dispenser	1	2.5%
Butcher	1	2.5%
Chowkidar	1	2.5%
Post master	1	2.5%
Total	40	100%

Table No.2: Clinical Presentation of BCC n=47

Nature of Lesion	Number of lesions	Percentage
Nodule	18	38.3%
Ulcer	18	38.3%
Flat Lesion	8	17%
Arising in a nevus	2	4.3%
Arising in a scar	1	2.1%
Total	47	100%

Table No.3: Distribution of Sites Affected by BCC n=47

Site	Number of Lesions	Percentage
Face – Nose	9	19.1%
Cheek	7	14.9%
Forehead	6	12.8%
Eyelid	3	6.4%
Face NOS*	9	19.1%
Back	4	8.6%
Ear	2	4.3%
Retroaural	2	4.3%
Chest wall	1	2.1%
Scalp	1	2.1%
Vulva	1	2.1%
Axilla	1	2.1%
Dorsum of Hand	1	2.1%
Total	47	100%

DISCUSSION

This was a retrospective as well as a prospective study. Therefore a major limitation was absence of clinical and epidemiological information in some of the retrospective cases.

Another limitation was that no long term follow up of patients could be done to assess the incidence of recurrence in our population.

Thirdly, in the absence of any radiological investigations, the presence or absence of metastases could not be commented upon.

In our study, we found a male predominance (65%), which concurs with Western and local studies^{4,5,6,7}. Another point of concurrence with other studies was the commonest age group affected. In our study, 75% of the patients with BCC were over 50 years old. Afridi et al's study in Northern Pakistan found the mean age of BCC patients to be 58.6 while a Yemeni study found the mean age of Non melanoma skin cancers to be 62.9 years^{5,8}. Other South Asian and Western figures also show that more than ¾ of the patients are above 40 years old^{4,6,9,10}. A recent European study found that the incidence of BCC among patients aged 80 years and older is high and increasing.¹¹

The majority of the lesions studied occurred on the face (72.3%), a finding which was similar to other studies⁸. On the face, the nose was the commonest site, a finding corroborated by other researchers^{1,12}. However, almost 15% (14.8%) occurred in areas which were not sun exposed (back, chest, axilla, vulva), supporting the contention that sun exposure is but one factor in tumourigenesis. BCC occurring in the axilla is rare but has been described in the literature¹³.

Vulvar BCC on the other hand, has been well documented^{14,15,16}. It has been found to occur most commonly as a nodulo-ulcerative lesion in post menopausal women, which was the case with our patient as well.

All 14 of the women in the study were housewives. Of these, half were village women who worked outdoors (history of chronic sun exposure). Of the remaining 26 male patients, there were 8 whose occupations were unknown due to lack of information. Of the remaining 18 patients, 13 (75%) had occupations involving prolonged sun exposure.

None of the patients studied gave any direct history of arsenic exposure. Arsenic is a known human carcinogen associated with development of BCC¹⁷. However, 4 (10%) of the patients were farmers and therefore more likely to have been exposed to arsenic containing insecticides. Also 7 (17.5%) of the patients were rural women who worked in fields and who would, therefore, have the same level of exposure to arsenic based insecticides as their male counterparts.

The commonest ethnic group affected by BCC was Punjabis (42.5%), followed by Pathans (20%). Again, the dearth of local studies on this subject gave no baseline for comparison.

A disconcertingly large proportion of patients presented with lesions of >5 years duration (40%). Only 10% of patients presented with <1 year history. The fact that most of our patients presented late could be attributed to the lower level of education, (only one out of 40 patients studied was a professional); the inaccessibility of health care services, and the reliance in our society on alternative treatments such as traditional healers. Other social factors such as poverty (no money for bus fare; not being able to afford to take the day off from work to go to the clinic), may have also contributed. The painless nature of the lesion could also have led to it being ignored. It is likely that only when the lesion persisted or grew larger, that medical advice was sought.

Three out of 40 patients studied had definite predisposing factors for the development of BCC. One patient was an albino with 6 lesions on various parts of his body. Albinos suffer from a lack of the photoprotective pigment melanin due to an inherited genetic defect resulting in markedly reduced (or absent) tyrosinase. This lack of melanin predisposes them to UV light induced damage and cancer¹⁸. Another patient had 2 BCC's on his forehead and histologically proven epidermodysplasia verruciformis and Bowenoid dysplasia elsewhere on his face. Epidermodysplasia verruciformis is associated with an increased risk of developing Non Melanoma Skin Cancers¹⁹. A third patient developed BCC 9 years after his mother also developed BCC. Studies of risk factors for cutaneous BCC found a significant association with family history of skin tumours²⁰.

CONCLUSION

We can conclude from the findings of our study that BCC in Karachi is not uncommon. It can be further noted that our study confirms the findings of other studies, which show that BCC commonly involves the sun exposed skin of elderly males usually as a nodulo-ulcerative lesion. Further studies may be done to

determine the effect of other factors, such as arsenic levels in soil and water in those places, which are found to yield high number of BCC cases.

Author's Contribution:

Concept & Design of Study: Shaima S. Memon
 Drafting: Pushpa Vali Ram
 Data Analysis: Nasimah Iqbal
 Revisiting Critically: Shaima S. Memon,
 Pushpa Vali Ram
 Final Approval of version: Shaima S. Memon

Conflict of Interest: The study has no conflict of interest to declare by any author.

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Impact of Acute Surgical Unit in Appendicectomy Outcomes

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Impact of Acute Surgical Unit in Appendicectomy Outcomes

ABSTRACT

Objective: To determine the impact of acute surgical unit in appendicectomy outcomes in our hospital.

Study Design: Prospective / cross-sectional study

Place and Duration of Study: This study was conducted at the SMBB Medical College and Sindh Government Lyari General Hospital, Karachi from January 2017 to December 2017.

Materials and Methods: The sample size of study was 100 taking prevalence to 32.5%. All patients with Age > 18 yrs, patients presenting with signs and symptoms of appendicitis in outpatient or emergency department were included. Patients with going home against advice and bleeding disorders were excluded.

Results: Out of 100 patients enrolled in study there were 45% males and 55% females. The mean age was 36.9 ± 9.67 years. Patients were shifted from emergency to theatre in 6.91 ± 1.22 hours, while the mean duration of hospital stay of patients was 2.95 ± 0.75 days. The complication rate in our study was 18%. Only 10% patients presented with negative appendicectomy.

Conclusion: Acute surgical unit is associated with decreased patients' morbidity due to early appendicectomy with decreased length of stay and postoperative complication.

Key Words: Appendicitis, Acute Surgical Unit, Outcomes

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INTRODUCTION

Appendicitis is a surgical emergency requiring hospital admission and ultimately surgery in 300,000 patients every year in US^{1,2}. In 2015 around 11.6 million cases have occurred with around 50100 deaths reported¹⁻³. In Pakistan studies have shown 37% incidence of appendicitis, around 22%-37% requiring appendectomy and postoperative complications developing in 33% patients^{4,5}.

Appendectomy is standard treatment and gives rise to complications if not operated with 3% developing complication in unruptured cases and 59% in case of rupture⁴⁻⁶. Laparoscopic appendicectomy have been favored over the open method in terms of lesser complications, shorter hospital stay, decreased admission duration which then impacts quality of life of patients with early resumption of normal activities⁶⁻¹⁰. Different studies have been done to determine outcomes of meta-analysis. Balasubramanian et al has compared 14 comparative studies and found that acute surgical units reduce chances of complications and improves quality of care⁷.

Kinnear et al has also compared acute surgical unit with traditional units improved ER to OT referral time of 19.4 vs 17.9 hrs, length of stay of 2.32 to 2.06 days⁸. Qayyum et al has found 25% patients undergoing open appendectomy out of 26% presenting with appendicitis⁹. Another retrospective study by Raja et al found reversion to open appendicectomy in 3.31%, 3.9% readmissions, complications rate of 1.3%, 20-72% discharges in < 24 hours¹⁰.

The aim of the study was to determine impact of acute surgical unit in appendicectomy outcomes in our society in order to improve and decrease patient's quality of health care as well as lesser hospital stay.

MATERIALS AND METHODS

This study is a prospective cross-sectional study conducted in SMBB Medical College Lyari and Sindh Government Lyari General Hospital, Karachi from January 2017 to December 2017. Informed consent was taken from patients or next of kin after approval from ethical committee board. The sample size of study was 100 taking prevalence to 32.5%. All patients with Age > 18 yrs, patients presenting with signs and symptoms of appendicitis in outpatient or emergency department were included. Patients with going home against advice and bleeding disorders were excluded. After admission relevant history and examination as done. The laboratory test included polymorphonuclear count, urine detailed report and ultrasound scanning and computed tomography. Finally the surgery is been performed.

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The findings at operation were uniformly described on a data collection form. All excised specimens were sent for histopathologic examination. They were reviewed by one of the authors, who were aware of the surgeon's preoperative judgment of the diagnosis or the primary pathologic report.

Patients time of arrival and operation time shift, length of hospital stay, complications rates, and ICU admissions were addressed.

Data was analyzed by statistical software package SPSS version 20.0. Continuous variable that is patient's age were expressed as mean $\pm$ SD. Qualitative variables will be expressed as frequencies and percentages.

RESULTS

Out of 100 patients enrolled in study there were 45% males and 55% females. The mean age was 36.9 ± 9.67 years (table 1). Patients enrolled were mostly in young age with incidence nearly equal in both males and females.

Patients were shifted from emergency to theatre in 6.91 ± 1.22 hours compared to patients shifted from emergency to ward and then operation theatre. The mean duration of hospital stay of patients was 2.95 ± 0.75 days. The duration was lesser in patients undergoing laparoscopic appendectomy compared to open appendectomy. The complication rate in our study was 18% due to late presentations of patients with peritonitis patients requiring open laparotomy. Only 10% patients presented with negative appendectomy and were found to have ovarian cyst 6%, ureteric stone 4%. The number of patients readmitted within <48 hours were n=6 patients. Overall there was no mortality reported in our study.

Table No.1: Patients mean age

Variables	Mean $\pm$ SD Frequency (percentages)
1. Age in years	36.9 ± 9.67 years
2. Referral to OT in hours	6.91 ± 1.22 hours
3. Length of stay in hospital in days	2.95 ± 0.75 days
4. Postoperative complication	18%
5. Negative appendectomy	10%

DISCUSSION

The acute surgical unit's concept aroused due to need for blunt and penetrating trauma surgeries which needs urgent surgeries and intervention^{1, 2, 10-12}. Emergency management has faced crisis in terms of non availability of surgeons, overcrowding, delays, delivering critical care, timely surgical evaluation by Surgeons and has led to arousal of acute surgical unit. Emergency departments unfortunately suffer increased difficulties with arrangement of surgeon's coverage on

call. The AHA survey of emergency services conducted a survey on availability of on call and thus found increased difficulty in arranging surgeons¹⁰⁻¹². Studies have shown that with availability of acute surgical units rates of night time appendectomy and improved negative appendectomy rates.

In our study the mean age of patient was middle aged 36-37yrs. However different studies have also found similar incidences of age however on contrary to our report in which females were greater than males. Earley et al has found difference in age of patients presenting and treated by acute surgical group and the ones compared with urgent appendectomy¹².

Overall decreased length of stay, decreased rates of complications have been reported by the patients underwent early appendectomy. In our study the patient's average time of shifting to operation theatre was decreased, thus decreased hospital stay have been found in patients treated by early surgical unit. Allaway et al has found statistically significant results (p value <0.001) with reduction night time surgery, similar complications rates and significant decrease in hospital stay when compared with established acute surgical unit. Different meta-analysis comparing 14 studies found statistically significant difference in decreased hospital stay, complication rates, perforation rates^{6, 10-12}. Waqar et al has found higher rate of complication of around 48% with 30% perforation in patients presenting with acute appendicitis and doesn't seek medical attention.¹³ Another study by Asad et al reported 23% complications rate of appendicitis misdiagnosed by physicians and thus delays in urgent medical care results in increased morbidity¹⁴.

CONCLUSION

Acute surgical unit is associated with decreased patients morbidity due to early appendectomy with decreased length of stay and postoperative complication.

Author's Contribution:

Concept & Design of Study: Ameer Ali Khaskeli
 Drafting: Ishak Soomro
 Data Analysis: Farhat Bano, Feroz Mahar
 Revisiting Critically: Ameer Ali Khaskeli, Ishak Soomro
 Final Approval of version: Ameer Ali Khaskeli

Conflict of Interest: The study has no conflict of interest to declare by any author.

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Induction of Post Operative Corneal Astigmatism in Single Step versus Three Steps Corneal Tunnel for Cataract Surgery: A Retrospective Study

Muhammad Afzal Bodla¹, Ali Afzal Bodla¹ and Mishal Tanveer²

ABSTRACT

Objective: Identify the best possible surgical technique in order to have minimum possible unwanted astigmatism, hence reducing the significant symptoms associated. Furthermore to identify the best possible techniques in reducing surgical trauma, early rehabilitation and better patient satisfaction.

Study Design: retrospective analysis

Place and Duration of Study: This study was conducted at the Bodla Eye Care and Multan Medical and Dental College, Multan from March to August 2018.

Materials and Methods: 65 post phacoemulsification cases was done. Cases were operated by a single surgeon using ALCON 2.8 disposable keratomes. Keratomes were not reusable and intraocular lens of choice was ALCON AcrySof IQ SN60WF, with optic size of 6.0 and overall length of 13.0 mm. Intraocular lenses were inserted using ALCON approved Monarch IOL delivery cartridges.

Results: Out of 65 eyes there were 38 male (58.4%) and 27 female (41.5%) patients. From clinical notes grades of nuclear sclerosis were gathered at the time of presentation which was Grade-1 nuclear sclerosis in (1 eyes), Grade - 2, (17 eyes), Grade-3, (33 eyes), Grade-4 (11 eyes), Grade-5 (3 eyes). Preoperative visual acuity was found to be 6/12 or better in 4 (6.1%), between 6/18 to 6/36 in 48 (73.8%) and 13 eyes (20%) had a preoperative visual acuity of counting fingers to perception of light. Post operative visual acuity improved between 6/6 to 6/12 in 56 eyes and in 9 eyes, improved to 6/18 to 6/60. from 1st week, 8th week, 12th week, and 24th week clinic visit.

Conclusion: This study included 65 eyes that had phacoemulsification with posterior chamber intraocular lens implant. All patients had a single step, straight corneal incision using standard single use keratome. A gradual reduction in post operative corneal astigmatism was observed over a period of twelve months as per data gathered. Astigmatic error ranged from 0.00 to -0.50 Dcyl in 26 eyes (40%), 0.50 to -1.00Dcyl in 25 eyes (38.4%) , -1.00 to -1.50Dcyl in 14 eyes (21.5%). Comparing to data available on two or three step corneal incisions, it was found at par infact significant less astigmatic error was noticed. Furthermore on the part of surgeon visualisation of intraocular structures is better and allows greater access to the incision.

Key Words: Corneal Astigmatism, Phacoemulsification, Refractive Error.

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INTRODUCTION

Every surgeon is responsible for inducing a certain degree of corneal astigmatism following cataract surgery.^{1,2} The purpose of this study is to determine how can we reduce the severity of problems faced by

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this necessary evil. There are a number of factors which influence this phenomenon.³ This includes incision size, its configuration that whether its single, 2 or 3 steps, location of incision relative to limbus and the presence or absence of steep axis on which incision is made.^{1,4} The ideal of all is a single step, less than 3 mm wide, temporally placed incision.^{2,5} Easy said than done, our decision is very much influenced by unavoidable factors, including right or left eye, size of the eye ball, ease of approach to limbus , corneal thickness, depth of anterior chamber, pre existing corneal pathology and above all presence of preoperative astigmatism.^{5,6} There are strong recommendations from various studies on placement of surgical incisions at the steep axes.^{4,6} The obvious rationale is that the corneal incision will result in the flattening of steep axes with a secondary steepness of axes at right angle to the site of incision.⁷

This will lead to a significant reduction of post operative corneal astigmatism.

Our study primarily focuses on the importance and surgical relevance of single step, straight incision in cataract surgery. Authors are of the view that this is the better choice among different techniques described in the literature previously.

MATERIALS AND METHODS

This is a retrospective, non comparative analysis of 65 eyes who underwent cataract surgery at Bodla Eye Care and Multan Medical and Dental College, Multan. Authors have ensured to rule out any bias and standardised the surgical practices for patients included in the study. All patients were operated by the same surgeon, using same disposable keratome to reduce any chances of discrepancy. Data was collected from the records spanning from first to 24th week ending in August 2018. All patients were operated using ALCON Infiniti microsurgical platform. There was an obvious difference in the degree of nuclear sclerosis as mentioned previously but that is unavoidable. This obviously can result in excessive use of phaco power leading to corneal wound burns. All patients with any pre and post operative complications especially wound burn were excluded from the study. Visual acuity was not a parameter measured in this study, hence co morbidities e.g retinal pathology and glaucoma patients were included in the data collection.

RESULTS

A special focus was made on wound architecture. Instead of a traditional two or three step corneal incision it was more of a single step stab incision. The size of incision in all cases was 2.8 mm. Phaco tip sleeve again was of the same size to allow proper closure of the wound during surgical manipulation. Steeper axes were used where possible as based on keratometry readings. Incision was made in the clear cornea but it was tried to slightly nick the limbal vessels. This was to allow a secure self sealing post operatively. Supero temporal quadrant was used in majority of cases. This was keeping in mind that most patients have an against the rule astigmatism and they benefit more from a temporally placed corneal incision. It was ensured to achieve for a symmetric incision. That roof and floor were approximately of the same size. A radial entry was ensured in order to achieve the best possible symmetry. Obliquely placed incisions are known to leak postoperatively with a significant unwanted post operative corneal astigmatism. Corneal tunnels made following single step entry were of adequate size to prevent any problems associated with short or unnecessary long tunnels.

DISCUSSION

Corneal incision is of pivotal significance in induction of post operative corneal astigmatism.⁸ In the literature, there is always an emphasis on placing the incision along the steeper meridian.^{9,10} It leads to a reduction in the keratometry readings on steeper axes making it more flat.¹¹ Elderly patients especially presenting with senile cataracts are known to have an against the rule astigmatism.¹² A superior approach can lead to further flattening of the flat meridian resulting in more post operative corneal astigmatism, hence should be avoided.^{10,12}

In our study there was an obvious increase in the corneal astigmatism post surgery as expected. Our reported post operative corneal astigmatism is in comparison and acceptance of various studies already published.¹³ Though our study is non-comparative but it does show an obvious benefit on two and three step corneal incisions which invariably are more prolonged. A superior corneal incision carries its own advantages.¹⁴ It is easier to perform as no change in sitting position for the surgeon is required.¹⁵ It does provide a physical support for surgeons hands on patient forehead. Moreover it is extremely difficult to convert a temporal approach to an extra capsular cataract extraction.¹⁶ Despite of all mentioned facts, in our study we tried to avoid the typical 12'O clock position, hence better postoperative outcomes in terms of refractive error.

Authors would also like to stress on the ability of surgeon to perform cataract surgery using a temporal approach due to its obvious advantages. Authors believe that using steeper axes as the site of incision can result in much reduced postoperative corneal astigmatism and more rapid and complete visual and systemic rehabilitation.^{17,18} Minimal invasiveness also help patients with functioning filtering blebs, on anticoagulant medications, dry eye syndromes and those going for combined surgery as trabeculectomy and Phaco.¹⁹

The possible complications that can be envisaged in single step tunnel are increased wound instability post operatively.²⁰ This can lead to endophthalmitis; iris prolapsed and flat anterior chambers.²¹ Authors in this study did not come across any of these complications. We believe with adequate measures as optimum wound hydration and checking for post operative leaks on the table following surgery can significantly reduce the burden of such complications.

Knowing that the ultimate result of the incision is corneal flattening along the meridian of the incision, the surgeon can exploit this by operating along the steep meridian, thereby permitting the wound healing process to reduce the patients pre-existing astigmatism.²²

Obviously, certain adjustments are required when moving the incision away from the superior meridian. The largest shift will be to a temporal incision, which will be used for eyes with preoperative against-the-rule astigmatism. Because the cornea is horizontally oval, the temporal limbus is located more posteriorly than the superior limbus.^{22,23} Therefore, the temporal incision, must be, bevelled more anteriorly into the cornea prior to entering the anterior chamber, for temporal incision, it is recommend that entry in anterior chamber should be 1.5 to 2.0 mm from the limbus.^{22,23} The corneal tissue is soft, flexible and compressible, that mean the dissection into clear cornea can be squeezed tight by pressure against the endothelium from within the anterior chamber.^{15,23} It is the pressure in the eye that closes the incision. The more pressure in the eye that closes the incision, the stronger the incision.

By choosing the suprot temporal limbus, for single step clear corneal tunnel formation, one can not only, have reduced postoperative corneal astigmatism, but it also helps, in changing against the rule to with the rule astigmatism, and reduces already existing corneal astigmatism.

CONCLUSION

In our study 65 eyes underwent suprot temporal clear corneal tunnel formation, and had a follow up of 12 months, showed corneal astigmatic error ranging from -0.00 to -0.50Dcyl (26 eyes), -0.50 to -1.00Dcyl (25 eyes), -1.00 to -1.50Dcyl (14 eyes), with gradual decrease in refractive error, over increase in postoperative period. Authors conclude that working at the temporal periphery not only, results in better patients satisfaction in the form of less postoperative corneal astigmatism, but also early rehabilitation. Furthermore, on the part of surgeon, working is relatively easier than going for a complete temporal approach. We did not come across any significant post operative complications related to a single step corneal tunnel formation.

Author's Contribution:

Concept & Design of Study:	Muhammad Afzal Bodla
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Conflict of Interest: The study has no conflict of interest to declare by any author.

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CONCLUSION

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RECOMMENDATIONS

When appropriate, may be included.

ACKNOWLEDGMENTS

List of all contributors who do not meet the criteria for Authorship, such as a person who provided purely technical help, writing assistance or department chair who provided only general support. Financial & Material support should be acknowledged.

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