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EDITORIAL

PROFESSIONAL DEVELOPMENT IN THE ERA OF COVID 19

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COVID 19 and its sequels have incited panic all over the globe for the past one and a half years. We heard of its economic impact and we saw it challenging our health care facilities. The world faced the loss of manpower and alongside the educational development got steady. Soon, it was followed by the realization and need for distance learning. The world saw a major change in the modes of communication with the symposia getting replaced by webinars, congress taking the virtual form, the group discussions getting diverted to zoom sessions whilst the old-school classrooms were restructured into google classrooms. The classic paper got replaced by the keyboard, the whiteboards became the laptop screens and teachers were suddenly digital. None the less, the learning did not stop and development continued in all walks of life in a reformed manner and at a new pace.

Brian Tracy pointed it out correctly by calling continuous personal and professional development "THE KEY" to the future. Continuous Professional Development in the easiest can be referred to as a process of building, maintaining, and later enhancing the skills, a continuous approach, set of ideas, and a group of techniques that are focused on self-learning and professional growth. [1] Development in every meaning is supposed to be a lifelong process, and when it comes to professional development during the COVID era, the paradigm shift from remote to digital learning gave it a new morphology. There had been a different school of thoughts about the new adaptations, some considered it the easiest approach to binge on the e-lectures of the international speakers while sitting on the comfortable couch of the lounge with no hustle of traveling across the countries and avoiding the physical exhaustion. Others labeled it as a constraint to the norm of interaction and discussion. [2] While the movement from traditional learning to online coaching and course delivery gained momentum, the field experience never lost its due importance. Virtual reality simulations came into play and were thought to serve as mechanisms to support the developmental process but the worth of real-time experience could not dropdown. Multi-perspective 360 video is relatively an inexpensive approach according to some, but the equity of access to the technology has been a concern. Digital tools foster active learning and allow for collaboration between synchronous and asynchronous sessions but the need for a healthy learning environment stays unaddressed. Digital escape rooms came into play but the homework gaps are yet to be filled. [3] The impact of remote learning was graded short-term by one school of thought while the long term and time-tested impact of the national development and learning areas were second to none.

If the virtual learning experience is considered per se, it improved for the last one year in terms of connectivity, servers, digital gadgets, assessments, certifications for positive reinforcement. The world experienced online examinations that were once rare, the digital teachers who were once challenged for e-teaching have now provided quality content. To begin with, the target audience which once was small later transformed into masses and engage people across the continents. The online teaching over time became qualitative and more interactive to ensure better delivery. The providers became more capable and robust while the users became technology-friendly.

The other side of the picture is equally bright with no existing replacement in terms of professional relationships, hands-on skills, real-time experiences, communication skills, constructive criticism, thought sharing, and all the interactivity that is a part of the conventional setup.

While many believe in the traditional processes, the global transition and digital backup have supported it enough to keep them running smoothly when the professional development was on the verge of compromise. Things, on one hand, are getting back to their original shape but we have been exposed to the reality of the virtual world

with its utmost importance. It might not be a replacement for the conventional trends but for sure is a very strong mode of continued development that can fill the gaps more with passing days to make it another phenomenal experience for the world in the days to come. As Henry Ford said, "Anyone who stops learning is old, whether at twenty or eighty. Anyone who keeps learning stays young. The greatest thing in life is to keep your mind young". So to keep our minds young, learning (professional development) has to continue whether online or via traditional means.

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ORIGINAL ARTICLE

DEPRESSION, ANXIETY AND STRESS LEVEL DUE TO COVID-19 PANDEMIC IN PATHOLOGISTS WORKING IN TERTIARY HEALTH CARE CENTRES OF PAKISTAN

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ABSTRACT

Objectives: To determine the level of depression, anxiety and stress in pathologists due to the Covid -19 pandemic.

Materials and methods: It was a Cross-sectional Analytical Multicenter Questionnaire-based study conducted from April 2020 to June 2020 including Pathologists working in Khyber Teaching Hospital and Pakistan Institute of Medical Sciences, Islamabad. Informed written consent was obtained and DASS-21 Questionnaire was administered. Data were analysed by SPSS**.** Levels of depression, anxiety and stress were determined and analysed by multiple regression mothod to predict depression anxiety and stress levels from demographics.

Results: Mean age of the study sample was 25-63 (37±8.75). There were 13(22.4%) males and 45(77.6%) females. Overall DAS score, mean depression, anxiety and stress score were 31.5±22, 8.7±9.1, 7.4±7.1 and 15.3±9 respectively. Females had a higher overall DAS score (U=156.5, p=.011), depression score (U=178.5, p=.032) and anxiety score (U=168.5, p=.029) as compared to males. Anxiety scores were highest in pathologists working in the microbiology section and lowest in those of the chemical pathology section (χ^2=8.13, p=.043). Multiple regression analysis showed that the female gender was significantly associated with a higher overall DAS score (β=13.69, p=.047) and stress score (β=6.10, p=.031) as compared to the male gender.

Conclusion: Pathologists working in the Covid-19 pandemic have a high level of mental distress and females have a higher level of psychological distress as compared to males. Implementation of mental support programmes for health care workers during pandemic situations is required to provide psychological support to health care workers.

Keywords: Anxiety, Covid-19, Depression, Pathologists, Stress.

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INTRODUCTION

In December 2019, there were reports of cases of a distinct type of pneumonia near the food market in Wuhan city of China. The disease was identified to be caused by the Coronavirus. It was named as novel Coronavirus disease-2019, abbreviated as Covid-19 by World health organization (WHO) [1, 2]. Spread of the The disease was not only in China but to every part of the world until it took the form of a pandemic [2, 3].

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Advanced technology and extensive use of social media has made it possible for the news and information to spread fast all over the world. When the news of the Covid-19 pandemic spread across the world, it created mental stress and fear among the general population [3]. Despite the Covid-19 pandemic, health providers like physicians and pathologists continued to provide health-related services in hospitals. This situation put them at increased risk of contracting the disease as compared to the general population[3]. Literature shows that 29% of the health care providers got infected while working in hospitals as the Covid-19 started [3].

Literature showed scanty knowledge about the virus and the spread of the disease at the beginning of the pandemic. Despite this, pathologists continued to provide diagnostic services in hospitals [1, 4]. The spread of infection to them and their families was the main concern [5]. These fears and worries lead to mental stress, anxiety and

depression in pathologists working in hospitals as they had to deal with patients and specimens like nasal swabs, blood samples and other body specimens[6].

It is reported that the majority of health care workers had already suffered from psychiatric problems during and after the severe acute respiratory syndrome epidemic in 2003 [7]. Middle East respiratory syndrome epidemic in 2015 also caused the health care workers to suffer from dysphoria and stress[7]. It was noted that the mental stress in health care workers persisted even after these epidemics ended. This shows that the mental effects on health care workers are long-lasting and may persist for long durations [8, 9]. Therefore, it is necessary to identify the health care workers who are having mental stress, anxiety and depression in this pandemic, so that they can be helped out by the provision of psychological support. It is necessary to identify and address the factors responsible for this stress. This is important as the psychological problems in health care workers may affect their work performance and impair their decision-making capabilities. This can cause pathologists to make diagnostic errors and which will in turn cause patients to suffer [3] . Therefore, the mental health of health care workers in the Covid-19 pandemic can be considered as a public health problem[3].

Pakistan is the country that is affected by Covid-19. The pathologists are continuously involved in providing diagnostic services to Covid-19 patients and the general population during the pandemic. Mental health affects the working ability. We conducted this study to determine levels of depression, stress and anxiety in pathologists in our region [6].

MATERIALS AND METHODS

It was a Cross-sectional Analytical Multicenter Questionnaire-based study which was conducted from April 2020 to June 2020 by including Pathologists working in Khyber Teaching Hospital, Peshawar and Pakistan Institute of Medical Sciences, Islamabad. Sampling was done using the non-probability consecutive sampling technique. The sample size was calculated by using an online sample size calculator taking confidence level as 95%, and margin of error as 5%. Ethical approval for the study was obtained from the Ethical review board. Informed written consent was obtained from the participants and the DASS-21 (Depression, anxiety, stress scale)

A questionnaire was administered to assess the mental health of Pathologists[10, 11]. The data analyzed using SPSS Chronbach alpha for depression, anxiety and stress sections of the questionnaires was .898, .709, and .886 respectively, while that for the complete DASS-21 questionnaire was .928. Cases were categorized on a depression scale a normal, mild, moderate, severe and extremely based on the score as per the DASS-21 questionnaire.

The normality of the data was analysed by the Shapiro Wilks test and visual inspection of histograms and Q-Q plots. Mean and standard deviation was used for quantitative data while frequency and percentages were used for qualitative data. The significance of the difference in scores between genders and marital status was determined by the Mann-Whitney U, while that for speciality and qualification with Kruskal Wallis test. Multiple regression analysis was done to determine the effect of gender, marital status, and speciality on DAS scores. In all the statistical procedures, the *p*-value of less than 0.05 was taken as statistically significant.

RESULTS

The Characteristics of the study population are shown in table 1. Different levels of depression, anxiety and stress are shown in figure 1. DAS scores are shown in table 2. Multiple regression analysis is shown in table 3.

DISCUSSION

Pathologists have worked in hospitals during the Covid-19 pandemic to provide diagnostic services to the of Covid-19 patients despite stressful circumstances [6]. Due to being exposer to the patient's samples and subsequent risk of contracting the infection, scarcity of protective equipment, and separation from families, pathologists suffered from psychological stress, which manifests as depression and anxiety[12]. Despite suffering from mental stress, most of the time the affected professionals do not seek psychiatric help which keeps the problem unsolved. A psychological crisis intervention plan needs to be developed such as the provision of online courses by psychiatrists for the guidance of health workers in a pandemic, giving pre-job training to identify psychological problems in healthcare workers and regular mental health surveillance programmes by a team of psychologists and counsellors, who should visit medical professionals to listen to their problems and provide support[6].

In the present study, the mean age of the study sample was 37±8.7 years. There was a predominance of females and married participants. Similar demographic data is reported in a study done by Elbay RY, where the mean age of the study sample was 36.05±8.69, females were predominant and the majority of the participants were married [13]. Similarly in another study done by Tan BY from Singapore, the mean age of the sample was 30 years, females were predominant as compared to males, and the majority of the participants were married [14]. Similar demographics are reported by Sandesh from Karachi and Si MY from China [1, 15]

In the present study, depression, anxiety and stress were seen in 36.2%, 37.9% and 44.8% pathologists respectively. Mean overall DAS, depression, anxiety and stress scores among the pathologists was 31.5±22, 8.7±9.1, 7.4±7.1 and 15.3±9 respectively. In a study

done by Elbay RY, 64.7% of study participants had depression, 51.6% had anxiety, and 41.2% suffered from mental stress[13]. In the same study, the mean DAS score was 19.04±12.93, while that for depression, anxiety and stress the score was 6.92±4.70, 4.67±4.21 and 7.46±4.85 respectively [13]. It means that depression scores are higher in pathologists in our study compared to that of Albay RY. In another study done by Zhu Z in China, depression, anxiety and stress were seen in 13.5%,24.1% and 29.8% of healthcare workers[3]. These figures are much lower than those in our study. In another study done by Sandesh R from Karachi, the overall mean score for depression, anxiety and stress were 18.12 ± 10, 19.01 ± 9.2 and 20.12 ± 12.0 respectively [1]. In a study done by Tan from Singapore, the overall mean DASS-21 scores among health care workers were lower than those in the present study[14]. This shows that the rates of depression, anxiety and stress in our pathologists are more as compared to other parts of the world.

In the present study, most of the participants had moderate depression (13.8% cases), moderate anxiety (19% cases), and mild stress (19% cases). These figures are comparable to those reported by Elby RY, where most of the participants had moderate depression (27.4% cases), mild anxiety (16.3% cases) and moderate level stress (15.6% cases)[13]. A similar pattern is reported from China[15, 16]. However, in a study done by Sandesh R from Karachi, most of the cases were in the severe category of depression, anxiety and stress [1].

In the present study, it was seen that as compared to males, females had significantly higher overall DAS score (U=156.5, p=.011), depression scores (U=178.5, p=.032) and anxiety scores (U=168.5, p=.029). Anxiety scores were highest in pathologists working in the microbiology section and lowest in those of the chemical pathology section (χ^2=8.13,p=.043). Multiple regression analysis showed that female gender was significantly associated with a higher overall DAS score (β=13.69, p=.047) and stress score (β=6.10, p=.031) as compared to the male gender.

Zhu Z from China also found that the female gender was associated with increased scores of depression, anxiety and stress[3]. Additionally, Zhu Z also reported a job duration of more than 10 years, history of mental disorder and chronic disorder as significantly related to stress[3]. However, we could not find the effect of the above-mentioned elements on the DAS score in our study. Elbay also reported female gender is more prone to stress and depression [13]. In our study, marital status had no significant association with DAS scores, however, Elby reports that married participants had a low overall DAS score[13].

In Pakistan, pathologists are having high levels of stress, depression and anxiety as compared to other countries even though the hospital management kept all the health care workers alert regarding the pandemic, its effects and preventive measures. There is a need to provide psychological support to the health care workers that are front line warriors against Covid-19, like pathologists, physicians and nursing staff. This can be achieved by developing teams that do regular surveillance of the staff and provide mental health education, psychological guidance and counselling to those who are prone to develop psychiatric problems [17, 18]. To make things simple, online surveys may be conducted to identify those who are having psychological problems, followed by online counselling by psychologists[19]. We could not assess the effect of so-

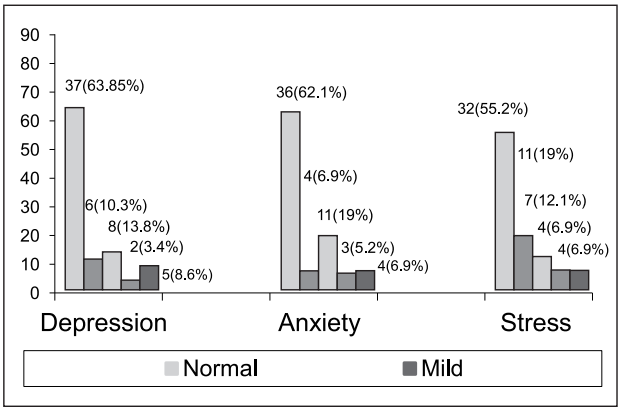

Fig 1: Gender distribution in study sample (n=101)

Table 1: Characteristics of the study participants (n=58)

Characteristics	Value		
Age in years (Range, Mean±SD)	25-63 (37±8.75)		
Gender	Males		13(22.4%)
	Females		45(77.6%)
Marital status	Married		49(84.5%)
	Unmarried		9(15.5%)
Qualification	M.B.B.S		8(12.8%)
	M.Phil		40(69%)
	F.C.P.S		9(15.5%)
	P.hD		1(1.7%)
Speciality	Haematology		22(37.9%)
	Chemical pathology		9(15.5%)
	Microbiology		10(17.2%)
	Histopathology		17(29.3%)
Mental status	Depression	Present	21(36.2%)
		Absent	37(63.8%)
	Anxiety	Present	22 (37.9%)
		Absent	36(62.1%)
	Stress	Present	26(44.8%)
		Absent	32(55.2%)

Table 2: DAS scores in study participants (n=58)

Scores			Mean±SD			Range	
Overall DAS score			31.5±22			0-106	
Mean depression score			8.7±9.1			0-34	
Mean anxiety score			7.4±7.1			0-36	
Mean stress score			15.3±9			0-42	
DAS scores concerning demographic characteristics							
Demographic characteristics	Overall DAS score	p-value	Depression score	p-value	Anxiety score	p-value	Stress score	p-value
Gender		.011		.032		.029		.074
Male	20.9±20.6	(U=156.5)	5±7	(U=178.5)	5.2±7.9	(U=168.5)	10.6±8.05	(U=197.0)
Female	34.6±21		9±9		8.04±6.8		16.7±8.9	
Marital status		.408		.369		.825		.590
Married	32.6±23.3	(U=182.0)	9.4±9.6	(U=179)	7.5±7.3	(U=210.5)	15.75±9.3	(U=195.5)
Unmarried	25.3±21.2		5.3±4.7		6.8±6.4		13.11±6.7	
Qualification		.394		.128		.747		.933
M.B.B.S	39.5±19.7	(X2=2.98)	13.7±6.9	(X2=5.63)	9.2±7.9	(X2=1.22)	16.5±9.05	(X2=.433)
M.Phil	30.3±23.2		7.8±9.4		7.5±7.5		14.9±9.1	
FCPS	30.8±20.3		9.3±9.1		5.5±4.4		16±9.8	
P.hD	24		4		4		16	
Speciality		.060		.367		.043		.166
Haematology	27.3±13	(X2=7.4)	6.5±5.8	(X2=3.16)	6.9±5.1	(X2=8.13)	14.6±6.02	(X2=5.076)
Chemical pathology	20.2±21.		6.8±9.7.		2.8±2.6.		10.4±10.1.	
Microbiology	40.4±29		10±9.4		11.2±11		19.2±11.04	
Histopathology	37.8±24		12±11.6		9.2±6.6		16.5±9.8	
P-value determined by Mann Whitney test and Kruskal Wallis test								

Table 3: Multiple regression analysis showing factors affecting DAS scores

Predictors	β	S.E	p-value	Confidence level	
				Lower limit	Upper limit
Overall DAS score					
Gender					
Male	-	-	-	-	-
Female	13.69	6.75	.047	.168	27.23
Marital status					
Married	-	-	-	-	-
Unmarried	-7.36	8.0	.361	-23.38	8.66
Speciality					
Haematology	-	-	-	-	-
Chemical pathology	-7.051.	8.45.	.408.	-23.9.	9.8.
Microbiology	13.12	8.14	.113	-3.20	29.4
Histopathology	10.61	6.89	.130	-3.2	24.4
Depression Score					
Gender					
Male	-	-	-	-	-
Female	4.790	2.83	.097	-.892	10.47
Marital status					

Married	-	-	-	-	-
Unmarried	-4.09	3.30	.220	-10.7	2.52
Speciality					
Haematology	-	-	-	-	-
Chemical pathology	.343	3.5	.924	-6.85	.7.54
Microbiology	3.45	3.4	.322	-3.98	16.39
Histopathology	5.45	2.92	.068	-4.18	11.32
Anxiety Score					
Gender					
Male	-	-	-	-	-
Female	2.81	2.23	.214	-1.672	7.29
Marital status					
Married	-	-	-	-	-
Unmarried	-.62	2.61	.813	-5.85	4.61
Speciality					
Haematology	-	-	-	-	-
Chemical pathology	-3.202	2.68.	.238	-8.58	2.18
Microbiology	5.71	2.58	.053	-.079	10.29
Histopathology	3.20	2.19	.150	-1.19	7.59
Stress Score					
Gender					
Male	-	-	-	-	-
Female	6.10	2.75	.031	.584	11.61
Marital status					
Married	-	-	-	-	-
Unmarried	-2.64	3.28	.424	-9.23	3.73
Speciality					
Haematology	-	-	-	-	-
Chemical pathology	-4.19.	3.5.	.238	-11.28	2.84.
Microbiology	4.56	3.38	.183	-2.22	11.34
Histopathology	1.95	2.86	. 499	-3.79	7.69

cioeconomic status, previous history of depression or anxiety in covid-19 patients. Secondly, we did not follow up with the participants to assess the duration for which the psychological effects persisted and whether they recovered or not. Thirdly, we did not determine post-traumatic stress disorder in pathologists.

CONCLUSION

Pathologists working in the Covid-19 pandemic have a higher level of stress, depression and anxiety in our region. The female gender is associated with higher rates of psychological distress. This warrants the initiation of psychological support programs and follow ups during emergencies like Covid-19 by the authorities to promote mental health in pathologists.

We recommend the initiation of psychological support programmes for the health care workers by authorities during emergencies like Covid-19. We suggest that follow-up studies should be done to see the progression and outcome of psychological problems in health care workers. Moreover, we recommend further studies to find out the cause of greater stress in females as compared to males in our population.

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AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under

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Khan MI:	Acquisition of Data and critical review
Shafi M:	Analysis and interpretation of data
Hussain Z:	Data collection, Bibliography
Khan HN:	Statistical Analysis
Rasheed H:	Writing of manuscript, proof reading

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

ORIGINAL ARTICLE

THE FREQUENCY OF HYPOKALEMIA IN PATIENTS WITH NASOGASTRIC FEEDING IN NON-HOSPITAL SETTINGS

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ABSTRACT

Objectives: To determine the frequency of hypokalemia in patients on nasogastric feeding with homemade blends and juices in non-hospitalized settings.

Material and Methods: The cross-sectional study was carried out in the General Medicine Department of Khyber Teaching Hospital, Peshawar from 1st January 2016 to 30th June 2016. There was a total of 176 patients in our study. We enrolled patients with oropharyngeal or esophageal dysphagia who were sent home on nasogastric tube feeding with homemade blends and juices. They were followed up after two weeks in the outpatient department, and their blood samples were collected for checking their serum potassium levels. Samples were tested using K-lite 5 series electrolyte analyzer at Khyber Teaching Hospital laboratory for the presence of hypokalemia.

Results: There were 98 males and 78 females in the study population. The mean age was 58.15 years ±13.35 SD. The mean value of potassium was 4.07 mmol/L ± 0.8 SD. In our study sample, we found hypokalemia in 31 (17.6 %) of the patients sent on nasogastric feeding at home.

Conclusion: Hypokalemia among patients with oropharyngeal and esophageal dysphagia who are on nasogastric tube feeding with homemade juices and liquefied blends for two weeks or more in a non-clinical setting was a relatively common finding irrespective of age, gender, or underlying disease. It is essential to recognize as it can be life-threatening.

Keywords: Hypokalemia, Nasogastric tube, Feeding.

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INTRODUCTION

Nasogastric (NG) tube feeding is a relatively common practice and is mainly used for patients with swallowing problems, particularly in the geriatric population. This procedure is relatively safe, and nasogastric tube feeding is used widely to support nutritional requirements in patients with an intact and functional gastrointestinal tract. Moreover, it is economical, relatively non-invasive, and easily manageable by healthcare workers compared to other enteral feeding options like PEG tubes and Jejunostomy. However, it can cause complications, including aspiration pneumonia, local trauma, diarrhea, and metabolic abnormalities.[1] Metabolic abnormalities associated with nasogastric tube feeding are quite common, and various studies have demonstrated its prevalence.[2] Hyperglycemia has been a well-documented abnormality associated with nasogastric tube feeding.[3]

Electrolyte imbalances can be life-threatening and can lead to fatal cardiac arrhythmias, neuromuscular disease, and myelinolysis of the pons if not recognized and managed promptly. [4, 5] Nasogastric tube feeding can cause GI irritation, vomiting, and diarrhea, and patients are predisposed to fluid and electrolytes disturbances. Hyponatremia, hypophosphatemia, hyperkalemia, and hypomagnesemia are associated with enteral tube feeding.[6,7]In our setup, there are limitations for options like jejunostomy tube and PEG tube feeding. Patients admitted in hospital with a stroke, swallowing disorders, and conditions that can impair consciousness remain on nasogastric tube feeding for long durations. This can predispose patients to electrolyte derangements, especially potassium, as it is present in high concentration in gastrointestinal secretions.[8] Hypokalemia is a possible complication and can be catastrophic as it can cause ventricular arrhythmias and neuromuscular weakness, leading to increased morbidity and mortality.[4,5]

It is usual practice to discharge patients home with nasogastric tube in situ and follow them up in the outpatient department for reassessment. There is no local study on the prevalence of hypokalemia in patients discharged home on nasogastric tube feeding using homemade juic-

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es and liquefied blends. Our study aimed to determine the frequency of hypokalemia in patients on NG tube feeding at home, which can help us formulate a protocol for identifying and managing hypokalemia promptly if prevalent in our setup and possible supplementation with potassium at home for its prevention.

MATERIAL AND METHODS

This descriptive, cross-sectional study was conducted in the Medicine department of Khyber Teaching Hospital, Peshawar. The study duration was six months, and it was conducted from 1st January 2016 to 30th June 2016. We started our study after obtaining approval from the institutional ethical committee. All Patients who had unsafe swallowing secondary to a cerebrovascular accident or were unable to take food secondary to dementia or esophageal dysphagia admitted to the medical unit were considered for this study. All patients with oropharyngeal or esophageal dysphagia were sent home on exclusive NG tube feeding with homemade juices and liquefied blends for 2 weeks. Patients having normal electrolytes on the day of discharge of either gender and age above 18 years were included in the study.

Patients with chronic kidney, chronic liver disease, patients on diuretics, ACE inhibitors, or Angiotensin receptor blockers, those with two episodes of diarrhea or vomiting on a single day in the last one week and in those who had abdominal surgery or a history of intestinal obstruction in the previous four weeks were excluded. A serum level of potassium less than 3.6 mmol/liter was labelled as hypokalemia. The feed included homemade blended/liquefied recipes.

Clinical assessment was done by taking history and detailed clinical examination. The procedure of blood phlebotomy was explained to participants before collecting samples. The blood sample was collected using a 5cc BD syringe with a 23 gauge. Patients were advised not to make a fist while collecting the sample.[9] We did not apply tourniquet for identifying veins. If needed, it was applied for less than a minute and removed immediately after determining needle in the vein during venipuncture.

A 3-milliliter blood sample was collected and transferred immediately in an evacuated blood collection tube containing heparin for proper serum collection[10] Plunger of the syringe was not pushed while transferring samples to tubes to avoid hemolysis for avoiding effects on extracellular potassium levels.[11]

Tubes were gently inverted a few times for proper mixing with heparin and immediately transferred to the laboratory. Every sample was analyzed within four hours at Khyber teaching hospital laboratory by a pathologist with a minimum of 5-year experience. Serum was analyzed for potassium levels using K-lite 5 series electrolyte analyzer.

Data was analyzed using SPSS-23. Chi-square test was applied after stratification of data to check any significant association of hypokalemia with gender and different age groups. A P-value of less than or equal to 0.05 was considered significant. Results are presented in the form of tables.

RESULTS

In this study, we observed 176 patients sent home on nasogastric feeding with homemade juices and liquefied blends, in which 98 (55.6%) were male, and 78 (44.4%) were female patients. The male to female ratio was 1.22:1. The average age was 58.15 years ± 13.35 SD, and patients were stratified into four groups according to age, as given in Table 1. Average Serum Potassium was 4.07 mmol/L ± 0.82 SD. (Table 1)

Hypokalemia in patients on nasogastric feeding was found in 31 (17.6%) patients, while 145 (82.4%) patients had normal potassium levels (Figure 1). Distribution of hypokalemia (serum potassium < 3.6 mmol/L) according to the age of patients on nasogastric feeding shows that old age patients were more prone than younger age but statistically insignificant difference when stratifying over various age groups.

Hypokalemia was found in one-fifth of the patients in the age range above 76-years which was 6 (20.6%), followed by 21 patients (18.1%) having 50-75 years of age. The finding was comparatively low in younger age groups with 3(13%) in the age range of 25-50 years and 1 (1.25%) in 18-25 years (table 2). Gender-wise presence of hypokalemia was almost equal with 14 (17.9%) of females demonstrating the abnormality compared to males

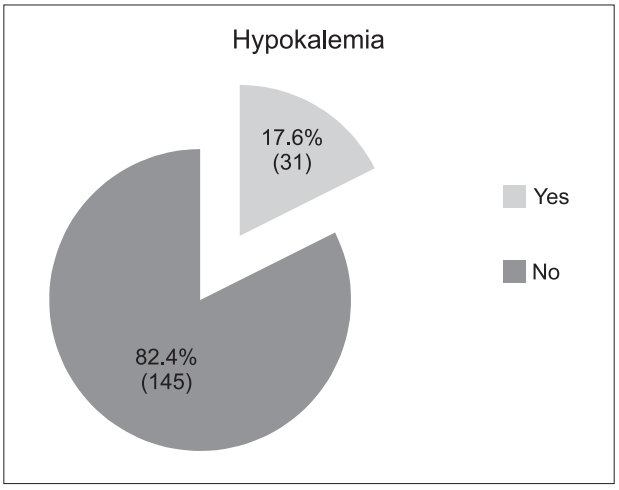

Fig 1: Hypokalemia distribution in the patients

Table 1: Age-wise stratification of the patients & mean values

Age in Years	Frequency	Percent
18 - 25	8	4.5
26 - 50	23	13
51 - 75	116	66
76 -100	29	16.5
Total	176	100.0
Age (Mean +SD	58.15 years ± 13.35	
Serum Potassium (Mean ± SD)	4.07 mmol/L ± 0.82 SD	

Table 2: Age-wise distribution of Hypokalemia

		Hypokalemia		Total	p-value
		Yes	No		
age (in years)	18-25	1	7	8	0.6835
		1.25%	98.75%	100.0%	
	26-50	3	20	23	
		13%	87%	100.0%	
	51-75	21	95	116	
		18.1%	81.9%	100.0%	
	76-100	6	23	29	
		20.6%	79.4%	100.0%	
Total		31	145	176	
		17.6%	82.4	100.0%	

Table 3: Gender wise distribution of Hypokalemia

		Hypokalemia		Total	p-value
		Yes	No		
Gender	Male	17	81	98	0.917
		17.3%	82.7%	100.0%	
	Female	14	64	78	
		17.9%	82.1%	100.0%	
Total		31	145	176	
		17.6%	82.4%	100.0%	

Table 3: Distribution of Hypokalemia in different disease groups

Indication for NG tube	Hypokalemia		Total	p-value
	Yes	No		
Cerebrovascular accident	17	90	107	0.751
	(15.8%)	(84.2%)	(100%)	
Dementia with oropharyngeal dysphagia including parkinsons	7	24	31	
	(22.5%)	(77.5%)	(100%)	
Oesophagal dysphagia including malignancy	5	18	23	
	(21.5%)	(78.5%)	(100%)	
Others	2	13	15	
	(13.3%)	(86.7%)	(100%)	
Total	31	145	176	
	(17.6%)	(82.4%)	(100%)	

17 (17.3%) Moreover, there was no significant difference in the distribution of hypokalemia among different diseases groups (table 3 and 4).

DISCUSSION

Hypokalemia is a complicated metabolic disorder and is well documented in patients on enteral feeding admitted to the hospital. Our main aim was to check the frequency of this electrolyte abnormality in patients sent home on nasogastric tube feeding. Our study showed that hypokalemia was present in 31(17.6%) of the study population after having two weeks of exclusive nasogastric tube feeding with homemade juices and liquefied blends at home. The finding of hypokalemia was not statistically significantly different among different age groups, gender, or different disease groups.

Pancorbo – Hidalgo, and colleagues did a study to see complications associated with NG tube feeding in the Internal medicine unit. They reported hypokalemia in 20.2 percent of the study population. It was relatively higher than our findings as it was performed in hospitalized patients. A study conducted in the Republic of Korea reported hypokalemia common in both elderly and non-elderly who had nasogastric tube feeding.[12] Sam Vanlandingham and his team evaluated patients on enteral tube feeding for metabolic abnormalities, and they found hypokalemia (8%), hyperkalemia (40%), and hyperglycemia (29%) in their study participants. Almost half of the study population in this study had a history of admission to ICU, which could probably explain such a high percentage of hyperkalemia.[2]

Oh HyanSoo and colleagues looked at the effect of feeding iso-osmolar formula via NG feeding in patients who had an acute stroke and demonstrated no significant effect on serum sodium and potassium level and attributed hyperglycemia to the stress effect of acute thrombotic event.[13] Enteral tube feeding with iso-osmolar formula did not significantly affect sodium and potassium levels. However, most participants had hyperglycemia before and after enteral tube feeding, indicating that hyperglycemia can be attributed to stress response related to acute brain infarction regardless of tube feeding. Another study showed metabolic complications in 2 percent of the study population on enteral tube feeding, and a majority had hyperkalemia rather than hypokalemia.[14] Metabolic abnormalities, including potassium imbalances, have also been reported in patients on long-term enteral nutrition at a nursing home on nasogastric tubes and PEG tubes feeding.[15, 16]

There have been inconsistent potassium level ab-

normalities in patients on nasogastric tube feeding, as evident from the above studies. Reasons could be a difference in participants, nature of their disease, feeding formulas used, and types of intravenous fluids therapy administered. Furthermore, GI intolerance is commonly associated with nasogastric tube feeding, which can lead to an increase in potassium losses in GI secretions and may have resulted in inconsistent potassium levels in different studies.[17] Our study population was different as they were followed up after having feeding at home. We excluded patients who had more than two episodes of diarrhea or vomiting on the same day. Lastly, comorbidities like chronic kidney disease and medications used by patients can affect the results of potassium levels and can lead to varying results.

We excluded confounders like medications, chronic kidney disease, and medications that could affect potassium levels for getting accurate results, but our study still had several limitations. We advised patients about diet plans at home. Still, compliance with that can't be assured because of the lack of community-based follow-up.[18, 19] Secondly, we mainly focused on potassium levels. It would have been better to assess for other metabolic abnormalities like glucose, sodium, magnesium, and phosphorous to have an overall view of metabolic abnormalities. Thirdly sample size was small because of time restraints that could limit results generalization to our population.

Studies can be done to check metabolic complications in addition to hypokalemia associated with enteral tube feeding at home. Such studies can provide a broader picture of various electrolytes and metabolites trends related to NG tube feeding. A larger study population on a standardized enteral feeding can provide further evidence on the association between hypokalemia and Nasogastric tube feeding.

We recommend educating patients and their caregivers about NG tube feeding because of the extensive range of biochemical problems and complications associated with enteral feeding. Moreover, a nutritional plan, type of nutritional supplements, and community services will help in identifying and preventing complications like hypokalemia related to nasogastric tube feeding at home.[18, 19, 20]

CONCLUSION

Hypokalemia among patients on nasogastric feeding in non-clinical setting is relatively common and essential to recognize as it can be life-threatening.

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AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under

Khan B: Concept/ Idea, Literature, review, Drafting & Final Review

Naeem A: Concept/ Idea, Analysis & Interpretation of Data, References

Naim F: Manuscript Writing, Literature review, Analysis & Interpretation of Data

Ullah K: Concept/idea, Data Collection

Wazir ZM: Concept/idea, Literature review, Drafting & Final Review

Khan N: Concept/idea, Literature review

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

ORIGINAL ARTICLE

BIOCHEMICAL PROFILE OF CHILDREN WITH ACUTE SEVERE MALNUTRITION AT A TERTIARY CARE SETTING

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ABSTRACT

Objective: The objective of this study was to explore the frequency of biochemical factors in children presenting with severe acute malnutrition.

Materials and methods: Children having an age range of 6-59 months with severe acute malnutrition of more than six weeks' duration, admitted at Pediatric Unit, Leady Reading Hospital Peshawar were included in the study. The study was conducted for 6 months (October 13, 2018, to April 13, 2019). The child's age, weight, mother's gestational age, mode of delivery, birth weight, maternal education, and parity were recorded on a proforma. Blood samples were sent to the hospital laboratory for serum electrolytes, hemoglobin, serum calcium, serum albumin, random blood sugar and the frequencies of these biochemical profile were calculated. Data were analyzed in SPSS-20.

Results: Out of 161 children, 48% were 1-3 years old, followed by 33% 3-5 years old. The majority of children were females (62%). Low birth weight children were 60%. Maternal illiteracy was 58%. Multiparty of mothers was reported in 59% and 67% of children were born by spontaneous vaginal delivery. Anemia was the most common (98%) finding followed by hypokalemia (68%), hypocalcemia (35%), Hypochloremia (16%), and Hyponatremia (14%). Serum albumin was low in 7% of children. Hypoglycemia was found in 15% of children.

Conclusion: Anemia followed by hypokalemia was the commonest biochemical findings in acute severe malnutrition. Similarly, hypocalcemia and hypoglycemia were also common life-threatening conditions found in these patients.

Keywords: Malnutrition; Severe acute malnutrition

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INTRODUCTION

The global population is expected to reach nine billion by 2050. Ensuring good quality food availability and food security is a global concern.[1, 2] Malnutrition is prevalent globally but especially in underdeveloped countries. Asia has around 70% of the world's malnourished children. [3] The situation is grave in four southeast Asian countries- Pakistan, Nepal, Bangladesh, and India. Though, some indices of nutritional assessment have improved from 1996-2011 in Pakistan, still there is much room for improvement. This particular improvement was noted for improvement in parental education, household income, and being born in a medical facility. [3, 4] According to WHO, malnutrition is responsible for 60% of deaths in children under 5 years of age. [2] For children younger than 5 years, severe stunting and wasting are responsible for 2.2 million deaths and resulted in 21% disability-adjusted life years (DALYs) in children under five years of age[3].

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Children with severe acute malnutrition (SAM) is a life-threatening condition and is responsible for 35% of mortality in children under 5 years of age. [5, 6] SAM results from a bout of severe acute illness, inappropriate child feeding, and acute severe shortage of food. [7] These children are nine times more likely to die than children without malnutrition. [8] Children with SAM have low immunity and are susceptible to infections with poor recovery. At the individual level, SAM is significantly associated with fever, vomiting, diarrhea, and being stunted. [7, 9] Infections further exacerbate malnutrition and a vicious cycle sets in. [9] Malnutrition has long-term effects on psychological development and cognition. [10, 11] At the domestic level, SAM is significantly associated with the handwashing habits of child's caregiver, malnourished parents, lack of toilets at home, and lack of diversity in family meals. Large family size and suboptimal feeding practices and food insecurity at domestic level practices also contribute as deter-

minants of malnutrition in children. [12, 13] Bottle feeding, prelacteal feeds, lack of exclusive breastfeeding and short duration of exclusive breastfeeding have been identified as significant contributors to malnutrition in children. [14]

In Pakistan, a national nutrition survey in 2011 reported under 5 years' children as wasted (13%), underweight (15%) and stunted (44%). [5] The 2018 national nutrition of Pakistan, reported stunting as 40.2%, with an increase in underweight children to 28.9% and rise in wasted under 5 years' children to 17.7%. [15]

Clinical signs alone are poor indicators of infection in SAM. The initial clinical diagnosis correlates poorly with diagnosis confirmed by radiologic, biochemical, and culture studies. The presence of SAM undervalues clinical signs. The biochemical, biologic, and radiologic parameters are of substantial value in SAM to support the diagnosis. This study was designed to explore the frequency of biochemical factors in children presenting with SAM.

MATERIAL AND METHODS

This descriptive cross-sectional study was conducted at the Department of Pediatrics, Lady Reading Hospital Peshawar from 13th October 2018 to 13th April 2019. A sample of 161 children was taken based on 7% proportion of malnutrition according to WHO sample size formula. A child was diagnosed with severe acute malnutrition (SAM) when the child weight for age Z score was < -3 using child growth standards as published by the World Health Organization (WHO) in 2006. [16]

Sampling was done by non-probability purposive sampling. Children with the age range of 6 to 59 months and SAM of more than six weeks were included in the study. Prematurely born children, with congenital anomalies, surgical problems, and systemic diseases were excluded from the study. On the day of admission, histories were taken and children were weighed. Infants were weighed on baby scales and children from 1 to 5 years were weighed on flat scales. The child's age, weight, gestational age, mode of delivery, birth weight, maternal education, parity was recorded on a proforma. Blood samples were analyzed in the hospital laboratory for serum electrolytes, hemoglobin, serum calcium, serum albumin, random blood sugar, and test results were analyzed.

Data were analyzed in SPSS-20. SAM was stratified among age, gender, birth weight, mother's parity, mode of delivery, mother education status, mother residence (rural or urban) to see the effect of this on the biochemical profile of malnourished children.

RESULTS

Out of 161 children, 48% of children were in the age range of 1-3 years, followed by 33% in the age range of 3-5 years. The majority of children with SAM were females (62%). The majority of children (60%) had low birth weight as shown in table 1.

Maternal illiteracy was common among mothers of children with SAM (58%). Multiparty of mothers was reported in 59% and 67% children with SAM were born by spontaneous vaginal delivery as shown in table 2.

Anemia was the most common (98%) finding in children with SAM. Among electrolyte abnormalities, hypokalemia was most common (68%) in children, followed by hypocalcemia (35%), Hypochloremia (16%), and Hyponatremia (14%). Serum albumin was low in 7% of children. Hypoglycemia was found in 15% of children as shown in table 3.

Table 1: Age, gender, and birth weight of the study population (n=161)

1	Age	Frequency	Percentage
	<1 year	31	19%
	≥1-3 years	77	48%
	>3-5 years	53	33%
	Total	161	100%
2	Birth weight		
	≤2.5 Kg	97	60%
	>2.5 Kg	64	40%
	Total	161	100%
3	Gender		
	Male	61	38%
	Female	100	62%
	Total	161	100%

Table 2: Maternal education, parity, gestational age, and mode of delivery of study population

1	Maternal education	Frequency	Percentage
	Illiterate	93	58%
	Primary	39	24%
	Secondary	29	18%
	Total	161	100%
2	Mode of delivery		
	Spontaneous vaginal delivery	108	67%
	Cesarean section	53	33%
	Total	161	100%
3	Maternal parity		
	Primipara	50	31%
	Multipara	111	59%
	Total	161	100%

Table 3: Biochemical profile of children with severe acute malnutrition

s/ no	Biochemical profile	Frequency	Percentage
1	Hyponatremia	23	14%
2	Hypokalemia	109	68%
3	Hypochloremia	26	16%
4	Hypoalbuminemia	11	7%
5	Hypoglycemia	24	15%
6	Hypocalcemia	56	35%
7	Anemia	158	98%

DISCUSSION

Worldwide, 165 million children below five years of age are malnourished, and this increases the likelihood of mortality in these children secondary to acute infections. At times, an acute infection sets grounds for acute malnutrition and sets a vicious circle of repeated infections.

Severe acute malnutrition may present with the signs and symptoms of the cause of SAM or any feature of deficiency resulting from SAM. Iron deficiency anemia in SAM is the most common finding as anemia is common in children under 5 years even without features of SAM. A study from India reported anemia in 81.1% as compared to 98% in this study, out of whom 25% required blood transfusion. Iron deficiency was most common followed by macrocytic anemia. [17] Anemia was reported as 53.7%, according to the 2018 national health survey of Pakistan[15]. Anemia was reported 19.5% in children admitted with SAM and acute infection in Niger. [9] A similar trend was observed in a study conducted by Thakur N et al. in which children with SAM are more prone to develop iron deficiency. [18]

The present study showed Hyponatremia in 14% of children which was more than a study conducted in India showing only 3%. [19] The reason could be that their sample size was very small. Some studies also reported a higher 28.6% of Hyponatremia as compared to present study. [9] Similarly, Hypokalemia was reported in a higher proportion (68%) in the present study as compared to 32.4% in a study from Niger. [9]

Hypoalbuminemia was reported in 7% in our study (2.0 ± 0.8 g/dl) while the Indian study showed 21% which was a higher proportion. [19] Hypoglycemia was reported in 15% (83 ± 28 mg/dl- mean ± SD) of children in our study which showed acute malnutrition in these children. Similarly, important micronutrient calcium was also deficient in these children which possibly lead to bone weakness. Hypocalcemia was seen in 35% which was more than the Indian study which was 15%. [19] These findings warrant special attention to assessment and management of the acute electrolytes and hypoglycemia management in children with SAM.

One of the limitations of this study is single-center data which may compromise the generalization of findings. Further multicenter studies of this kind are needed to find the true prevalence of biochemical abnormalities in SAM babies.

CONCLUSION

Acute severe malnutrition is a life-threatening condition. Anemia followed by hypokalemia was the commonest biochemical findings in acute severe malnutrition. Similarly, hypocalcemia and hypoglycemia were also common. Deficiency of all these micronutrients can lead to long-term complications and growth retardation. The condition needs aggressive nutritional replacement supplementation to prevent the long-term complication of nutrition deficiency.

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Following authors have made substantial contributions to the manuscript as under

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FREQUENCY OF RAISED BLOOD PRESSURE / RAISED MEAN ARTERIAL PRESSURE ABNORMALITIES IN PATIENTS WITH PRIMARY OPEN-ANGLE GLAUCOMA

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ABSTRACT

Objectives: To find out the frequency of raised blood pressure and raised mean arterial pressure in patients presenting with primary open-angle glaucoma

Material and Methods: This cross-sectional descriptive study was conducted in Khyber Teaching Hospital Peshawar from July 2020 to December 2020. All patients having primary open-angle glaucoma were included. Those having high blood pressure (BP) on admission or history of high blood pressure or using anti-hypertensive drugs, were admitted to the Ophthalmology ward of Khyber Teaching Hospital. Blood Pressure/ Mean Arterial Pressure and Intraocular pressure (IOP) phasing were done and Mean Arterial Pressure, MOPP, and peak IOP were determined. Patients having secondary types of glaucoma, primary angle-closure glaucoma, and those patients who declined consent were excluded. Data was collected on a proforma and analyzed by SPSS-23.

Results: A total of 375 patients were diagnosed to have Primary open-angle glaucoma (POAG), out of which 200 (65%) patients had impaired blood pressure. The rest of 70 (35%) patients had Normal-Tension Glaucoma (NTG). Out of 200 cases with primary open-angle glaucoma, 175 patients (87.5%) had hypertension, while 25 patients (12.5%) had low blood pressure (normal BP or low BP). Amongst the hypertensive patients, the mean arterial pressure (MAP) was raised in 70 (35%) patients, while the Mean Ocular Perfusion Pressure (MOPP) was raised in 15 patients i.e. 7.5%.

Conclusion: Amongst 65% of our patients with primary open-angle glaucoma, 87.5% of patients had high blood pressure, While the rest of 35% had

Keywords: Primary open-angle glaucoma (POAG), Impaired Blood Pressure, Impaired Mean Arterial Pressure.

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INTRODUCTION

Glaucoma is the leading cause of irreversible blindness or visual impairment. Approximately 60 million people worldwide are suffering from glaucoma[1]. Primary open-angle glaucoma (POAG) is an ocular disease characterized by optic neuropathy, changes in the optic disc and retinal nerve fiber layer (RNFL), and visual field defect with etiology still not properly evident. Though currently Intraocular pressure (IOP) is not included in its definition but is still considered the most important risk factor. If POAG is associated with elevated IOP of more than 21 mmHg, is labeled as high-pressure glaucoma, but if the IOP is normal, the POAG is labeled as Normal-Tension Glaucoma (NTG)[2].

Mean arterial pressure (MAP) is the average arterial pressure throughout each cardiac cycle, systole, and diastole. Normal MAP is 93 mmHg, ranging from 70 to 100 mmHg. Though ophthalmodynamometry is the classical method to measure the MAP in the central retinal artery (CRA)[3,4,5]. As it is not a very convenient method, so an alternative method based on mean Brachial artery blood pressure (MAP) is used[6], by applying a formula in which the Diastolic blood pressure is doubled, added to systolic blood pressure, and the composite is divided by 3. As variabilities in blood pressure and mean arterial pressure impairs the perfusion in the retina, and ultimately leading to primary open-angle glaucoma, so we wanted to determine this effect in our patients who presented to us with primary open-angle glaucoma.

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MATERIAL AND METHODS

This cross-sectional descriptive study was conducted in Khyber Teaching Hospital, Peshawar from July 2020 to December 2020, after approval from the ethical committee of Khyber Teaching Hospital, Peshawar. All patients having primary open-angle glaucoma were included. Consecutive sampling was done from patients attending the outpatients' department of the hospital and having POAG in one or both eyes. Those having high blood pressure (BP) on admission or history of high blood pressure or using anti-hypertensive drugs, were admitted to the ophthalmology ward of Khyber Teaching Hospital. Blood Pressure/ Mean Arterial Pressure and Intra Ocular Pressures (IOP) phasing was done. Mean Arterial Pressure, MOPP, and peak IOP were determined. Patients are known to have secondary types of glaucoma, primary closed-angle glaucoma, and those patients who declined consent were excluded. Data was collected on an already prepared standard proforma and was analyzed by SPSS 23.

RESULTS

A total of 375 patients were diagnosed to have Primary open-angle glaucoma (POAG), out of which 200 (65%) patients had a history of raised blood pressure, while the rest of 70 (35%) patients had Normal-Tension Glaucoma (NTG).

Out of 200 cases with primary open-angle glaucoma, 95 patients (47.5%) had a history of hypertension and were using antihypertensive drugs, 80 patients (40%) were newly diagnosed as hypertensive in the ward after admission, while 25 patients (12.5%) had normal blood pressure (Table 1). Amongst the hypertensive patients, the mean arterial pressure is given in Table-2.

Table 1: Abnormal blood pressure in patients with POAG.

B.P. anomaly	Frequency	Percentage
Hypertensives	95	47.5
Newly diagnosed hypertension.	80	40
Normotensive	25	12.5

Table 2: Mean Arterial Pressure in patients with hypertension with POAG

MAP	Frequency	Percentage
110 mm Hg plus	30	15
100 to 109 mmHg	40	20
99 to 90 mmHg	50	25
89 to 80 mmHg	55	27.5
< 80mmHg	25	12.5

DISCUSSION

Just like hypertension which is the silent killer of life, POAG is the silent killer of vision. In both of the diseases, the vasculature of organs is affected. POAG is the disease of the optic nerve and retina. If the vascular supply to the optic nerve is disturbed due to ischemia or raised IOP, it leads to optic neuropathy with typical glaucomatous visual field defect. Thus there is an association between perfusion, BP/MAP, and IOP. In hypertension, the IOP is elevated, as the aqueous humor secretion is increased due to increased hydrostatic pressure in capillaries of the ciliary body while aqueous humor outflow is decreased due to increased venous pressure in episcleral veins[7], while hypotension causes ischemic damage leading to NTG[8]. Of our patients, out of 375 patients with POAG, 200 (53.30%) had abnormal BP/MAP. As far as the general population is concerned hypertension has been recorded in 26.73% in the urban and adult population in 21.03% in rural adult population[9]. It means there must be a positive relationship between abnormal blood pressure and POAG, as compared to people with no primary open-angle glaucoma. Dave A et al from India have reported the frequency BP abnormalities in 47.03% of patients with primary open-angle glaucoma[10]. So the frequency was almost the same in both the neighboring countries. On the other hand, the frequency of POAG incidence was 2% in hypertensive patients as compared to the normal population at 1.7%[11]. In hypertensive patients, the incidence of POAG is higher when systolic BP is more than 140 mmhg[11]. Treatment with an appropriate dose of antihypertensive medication delays the onset of POAG[12], while uncontrolled hypertension was found a major risk factor for POAG as hypertension causes microvascular damage of the optic nerve and RNFL[13-16]. Pakharel S et al from Nepal have reported a strong positive correlation of POAG with increasing age, male gender, and low diastolic pressure[17]. Fasih et al have also reported that high systolic BP, diastolic blood pressure, and raised IOP in patients with POAG[18]. Increased intraocular pressure and high blood pressure were also reported by Sadiqullah et al[19] and several other international studies [20-24]. A famous epidemiological study conducted from 1990 to 2019 and comprising of fifty thousand patients by Grzybowski A et al. concluded that hypertension and blood pressure dipping were important risk factors for glaucomatous optic neuropathy and its progression[25].

CONCLUSION

Sixty-five percent of our patients with primary open-angle glaucoma had impaired blood pressure, out of which 87.5% of patients had high blood pressure and the rest had normal blood pressure. So we recommend that patients with hypertension must be screened for POAG and vice versa.

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AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under

Khan BS: Concept/ Idea, Literature, review, Drafting & Final Review

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ORIGINAL ARTICLE

MATERNAL HEALTH CARE IN TERTIARY HOSPITAL IN TERMS OF MATERNAL NEAR MISSES (MNM) INDICATORS

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ABSTRACT

Objective: To assess maternal health care in terms of maternal near-miss indicators i.e., maternal near-miss rate, Maternal Near Miss to mortality ratio, and Maternal Mortality Index in tertiary care, Lady Reading, hospital.

Materials and Methods : It was a cross-sectional descriptive case study conducted in Obstetrics A unit of Lady Reading Hospital from January 2019 to December 2019. The WHO near-miss "severe maternal complication" based inclusion criteria was used for case identification. The study population consisted of all women who were admitted during pregnancy, labor, or within the first 42 days of postpartum to our unit. The outcome was measured using the three indicators i.e. the mortality indices of near misses, maternal mortality ratio, mortality to near-miss ratio, near-miss cases/1000 deliveries

Results: The total number of admissions in the department in the year 2019 was were 10439. The total Maternal Near Miss cases were 1776 (1.84%). Maternal Near Miss Rate was calculated as 170 per 1000 live births. There were 44 total maternal deaths, and the maternal mortality rate was calculated as 421 per 100,000 live births. The Maternal Near Miss to Mortality ratio was 41:1. The mortality Index was 2.5%.

Conclusion: Our hospital has a higher maternal near-miss to mortality ratio of 41:1 showing good maternal care management.

Keywords: Maternal near-miss, Near-miss indicators mortality index, Maternal mortality.

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INTRODUCTION

Maternal near-miss is defined as "a woman who nearly died", in other words, she survived a complication that occurred during pregnancy, childbirth, or within 42 days (6 weeks) of termination of pregnancy. [1] The risk of maternal death is 1 in 41 live births in developing countries to 1 in 3300 live births in developed countries respectively. For every woman who dies, 20 more women experience acute and chronic complications. [2,3] Between 1990 and 2015, the global maternal mortality ratio has decreased by 44%, although the decrease differed substantially among regions, with the highest decrease in eastern Asia 72% still 99% of the contribution to world maternal death is from developing region. [4]

Although maternal mortality has been used to assess the quality of obstetric care, there is a lack of standard definitions and criteria for identifying severe maternal morbidity and near-miss. Near miss cases share many characteristics with maternal deaths and can directly inform about various obstacles to care, which can help in understanding the current health care system. [5,6] In addition, auditing near miss cases can be seen as the success of healthcare workers, as great saves. [7,8]

World Health Organization (WHO) has developed a new definition of maternal near-miss (MNM) and formulated identification criteria for maternal near-miss cases in 2009 using 3 categories: clinical, laboratory-based, and management-based criteria. [9] The development of the near-miss criteria resulted in the development of the "2011-WHO near-miss approach". [10] This approach is a guideline for evaluating the quality of care for severe pregnancy complications, based on the concept of criterion-based clinical audit. [11]

According to WHO, the prevalence of severe maternal outcomes (maternal death and maternal near-miss) is expected to be 7.5 per 1000 live births. [13] It ranges from 0.6 to 14.98 % by disease-specific criteria and 0.04 to 4.54 % by the management-based criteria. The magnitude of a maternal near-miss is high among African and Asian middle and low-income countries. [12] A systematic review by WHO also showed that the prevalence of severe maternal morbidity (near-miss) varies between 0.80–8.23 % among studies that used disease-specific criteria and 0.01–2.99% among studies that used management-based criteria. [13] This study reports WHO near-miss cases criteria from a tertiary care hospital from Pakistan (a lower-middle-income country), where the burden of maternal mortality and morbidity is

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high.

MATERIAL AND METHODS

This was a cross-sectional study which was conducted from January 2019 to December 2019 in Obstetrics and Gynecology (OBGYN) department at Lady Reading Hospital (LRH), which is a large tertiary care hospital in Peshawar Pakistan. We included all maternal deaths and maternal-near-misses that were admitted to the OBGYN unit during the above-mentioned period. In this study, a maternal death (MD) is defined as the death of a woman while pregnant or within 42 days of termination of pregnancy, from any cause. For the identification of maternal near misses, we used the WHO near-miss criteria, which include the obstetric diagnoses of hypertensive disorders (severe preeclampsia, eclampsia), severe hemorrhage, dystocia (defined in the current study as uterine rupture, impending uterine rupture like prolonged labor with previous cesarean section, and emergency C/S delivery), severe anemia (Hb < 6 g/dl), and sepsis (puerperal sepsis, chorioamnionitis, and septic abortion).

The study protocol was approved by Ethical Review Board of the hospital. Due to the majority of the participants being uneducated, verbal informed consent was directly obtained from study participants after explaining the study. The following near-miss indices /indicators were calculated.

(1) MNM incidence ratio refers to the number of maternal near-miss cases per 1,000 live births (LB). (MNM IR = MNM/LB).

(2) Maternal near miss: mortality ratio: Proportion between maternal near-miss cases and maternal deaths. A higher ratio indicates better care. (MNM: 1MD.)

(3) Mortality Index: Number of maternal deaths divided by the number of women with life-threatening conditions, expressed as a percentage. The higher the index, is more women with life-threatening conditions die (low quality of care), while the low index suggests better quality of health care. (MI = MD/(MNM + MD) × 100. Data were entered using SPSS version 21 for analysis. Descriptive statistics like frequencies, proportions, median, and mean were used to explain important variables to the outcome variable

RESULTS

The total number of admissions in the department in the year 2019 was were 10439, 15.83% were booked and 84.16 % were un-booked/referred patients from local private and government hospitals in Khyber Pakhtunkhwa. The total number of MNM seen was 1776 who fulfilled the inclusion criteria. Maternal deaths were 44 in the year 2019. Below is a table-1 of the different maternal near-miss and their frequency. The MNM was 1776 (1.84%). The ratio of near-miss events to maternal deaths was 41 to 1. The mortality Index for near-miss cases was 2.5% (table 2).

Table 1: Total maternal admissions and maternal mortality indicators

Total Admission	Frequency N= 10439
Total Maternal Near Miss(Mnm)	1776 (1.84%)
Maternal Near Miss Rate	x 1000= 170 per 1000 live births
Maternal Deaths	44
Maternal Mortality Rate	x 100,000 = 421 per 100,000 live births
Maternal Near Miss To Mortality Ratio	1776:44 (41:1)
Mortality Index	x 100= 2.5%

Table 2: Causes of Maternal Near Miss displayed as percentage

Causes oF Maternal Near Misses(MNM=1776)	Percentage%
Hypertensive disorders	27.08%
anemia	48.76%
Dystocia	20%
Severe hemorrhage	4%
Maternal septicemia	1%

DISCUSSION

Our results showed that the MNM from Peshawar was 17.67% or 170 per 1000 live births. Comparing MNM rates can be challenging due to a variation in the criteria used for identifying MNM. Our percentage is higher than that provided by Tunclap et al in their systematic review of 2012. Based on their results when disease-specific based criteria were used, the prevalence of MNM was between 0.60% to 14.98%, which is the criteria we used. [14]

A similar cross-section study was done in India by Adisasmita et al where they reviewed public and private hospital records between 2003-2004 and reported the prevalence of MNM. They noted a higher MNM prevalence in public hospitals 17.3% compared to private 4.2%. Our findings are consistent with their study because we depict MNM from a public hospital, our MNM prevalence was higher 17.6%. [15]

Morse et al. have reported MNM from a regional hospital in Brazil. They found 89 MNM out of the total 1544 cases. Their results were between 81 to 9.4 per 1000 live births based on the criteria used. Our MNM is based on disease-specific criteria and is consistent with the prevalence range provided by Morse et al. Morse et al used three different criteria to report the range of findings. Our MMR of 41 per 1000 was substantially higher than their MMR of 3.2 %. While comparing causes of MNM we noted a stark difference in the causes. The major cause of maternal morbidity in Brazil was Preeclampsia, while in our study from Pakistan the top cause of MNM was anaemia. [16]

WHO criteria of MNM ratio (MNMR) mentions the

number of maternal near-miss cases per 1000 live births (LB). This criterion is being reviewed to improve the quality of care because a large number of MNM cases will experience long-term physical and psychological effects. [17] The maternal near-miss ratio (MNMR) in our study was 170 /1000 live births in our study. This finding is consistent with results from other lower-income countries which show a range between 2.2 to 287.7 /1000 Live birth. [18]

The maternal mortality rate MMR calculated based on our results was 421/100,000 live births. The average maternal mortality rate in Asia-Pacific is reported to be 127 per 100,000 live births, compared to the developed-country average of just 12 per 100,000. [19] The lower middle income countries including Pakistan, Afghanistan, and Bangladesh, have particularly high maternal mortality rates, reaching up to 423/100000 live births.

When the causes of Maternal Mortality were evaluated, Eclampsia was the leading cause of death in our study. Secondary causes were pulmonary embolism, postpartum hemorrhage, and septicemia. Literature shows that hemorrhage is the leading cause of maternal deaths in Africa (33.9%) while in Asia (30.8%) Latin America and the Caribbean, hypertensive disorders were the primary etiology of maternal mortality. [20]

The near-miss to mortality ratio was 41:1, which means for every 41 mothers who experiences life-threatening conditions, there was one mother who died. In other words, for every 41 mothers who got sick, 40 mothers were saved while 1 mother died. This indicates better obstetric care. The MMNMR based on a study from Syria shows a ratio of 60: 1, while a study done in Nepal showed a ratio of 72: 1. [11,12] This ratio is similar to those of African countries where the range is 15–12. [18] This is a far cry from those reported in Western Europe. Their studies have reported a ratio of 117–223: 116. If this ratio increases over some time, it reflects on the improvement achieved in obstetric care. So instead of a single estimation, the yearly estimation may help us in improving the care provided. The major contributor to maternal near misses and direct maternal death in our unit was hypertensive disorders (27.04% near misses) with the majority presenting with eclampsia (201 patients) with complications like HELLP syndrome, pulmonary edema requiring assisted ventilation, and intracranial hemorrhage. Of the indirect causes of severe maternal outcomes, anemia was the most common 48.78% in this study with 75% of patients having nutritional iron deficiency anemia. These poor reserves of iron made them prone to severe anemia in pregnancy and presented to us as late booker which required multiple blood transfusions. Beta thalassemia is at its highest incidence in KPK with 2-8% incidence. Patients are diagnosed for the first time in pregnancy when they presented with severe anemia in the antenatal visit. Anemia in pregnancy was also noted in the WHO MCS study as well as in other studies in developed countries to be the indirect leading cause of maternal near miss. [21,22]

The third category of the near-miss was dystocia which was 20%. The majority included c/section of patients who were referred from the periphery with obstructed labor or prolonged 2nd stage of labor (303 patients), contributing to an increased rate of c section in this unit of 25.76%. Subtotal hysterectomy was done for the atonic uterus leading to PPH in 29 cases and ruptured uterus in 19 patients. A morbidly adherent placenta was seen in 9 patients for which total abdominal hysterectomy was done. These cases are now on the verge of the increase due to the increasing number of c/section being done leading to a high number of blood product transfusions and ICU admissions. This point is of importance to note, of exploring the negative impact of high C-section rates on maternal health. Internationally, studies have documented the association between the increased incidence of placenta previa and accreta with the increase in cesarean delivery rates and the number of previous ones. [23,24]

It was noted that the majority of women in this study were unable to seek medical care in time leading to an exaggeration of risk factors and an increase in morbidity that can be easily addressed had it been managed timely. Of the many reasons for delay from the periphery is the long-distance travel to reach health facility and delayed referral to most appropriate health facility. So, it is important to Improve the timely healthcare-seeking behavior of women.

CONCLUSION

Our hospital has a higher maternal near-miss to mortality ratio of 41:1 showing good maternal care management. Timely healthcare-seeking behavior of women is uncommon in the study area, therefore, a considerable number of women are developing severe acute maternal morbidities that can be easily addressed had it been managed in a timely manner.

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Following authors have made substantial contributions to the manuscript as under

Zahoor F: Concept/ Idea, Literature, review, Drafting & Final Review

Fahim F: Concept/idea, Literature review, Drafting & Final Review

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

ORIGINAL ARTICLE

COMPARATIVE EVALUATION OF 70^{O} AND 90^{O} RIGID ENDOSCOPE IN SUCCESSFUL VISUALIZATION OF THE HIDDEN AREAS OF LARYNX

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ABSTRACT

Objective: To compare the success rate of 70^{0} and 90^{0} rigid endoscopies in successful visualization of the hidden areas of the larynx.

Material And Methods: A randomized control trial at Otorhinolaryngology-Head and nack surgry department PIMS Islamabad from May to November 2018. Written informed consent from 582 patients fulfilling the inclusion criteria was enrolled from the outpatient department (291 in each group). They were randomized into two groups using a computer-generated table. Patients in Group A underwent the procedure using 70^{0} rigid telescopes and those in Group B using 90^{0} rigid telescopes. The following parameters were evaluated: anterior commissure, the laryngeal surface of the epiglottis, and subglottis.

Results: A total of 582 patients were included in the study. The mean age (years) of patients was 38.88+12.71. 267 (group A) and 251 (group B) patients successfully visualized the subglottic area, whereas 261 and 239 patients from group A and B respectively, were successfully visualized with anterior commissure. Similarly, the successfully visualized laryngeal surface of the epiglottis is 273 and 240 respectively for 70^{0}& 90^{0} scopes.

Conclusion: The study findings concluded that the rate of success of 70^{0} rigid endoscopes was more successful in the visualization of the hidden areas of the larynx as compared to 90^{0} rigid endoscopes.

Keywords: Full Visualization of Subglottic, Anterior Commissure, Laryngeal Surface of Epiglottis, telescope, 70^{0}, 90^{0}endoscopes

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INTRODUCTION

Laryngeal framework is complex which is anatomically comprised of several mucosal folds, elastic membranes, ligaments, and muscles constructed on the cartilaginous framework. In modern health care, pathologies of the upper aerodigestive tract represent the main problem.[1]To establish an exact histopathological diagnosis, diagnosis of laryngeal pathology including its site, size, extensions, and adequate tissue for biopsy is required[2]. Malignant lesions require correct staging and it carries great importance in treatment planning.[1] In order to detect the pathology in the larynx various procedures can be used like Indirect Laryngoscopy, Direct Laryngoscopy, and Endoscopic examination. For evaluation of laryngeal lesions, indirect laryngoscopy has the main role in identifying glottic and supraglottic lesions, but there are some areas that are not optimally examined, so examination remains less accurate and incomplete[3]. Direct laryngoscopy can be used for biopsy it requires general anesthesia, and depends on the surgeon's expertise[1]. Endoscopic tools for examination of the upper aerodigestive tract have undergone significant developments in recent years and have revolutionized the way of diagnosis and management of upper aerodigestive pathologies.[4-6]

In the study by Jun Shao, Jennifer Stem, Zheng-Min et al[7] the 70-degree scope provided successful visualization of the subglottic area in patients (91.7%), of Anterior commissure in(92.6%)and on the laryngeal surface of the epiglottis in (94.2%). The 90-degree scope provided successful visualization of the subglottic area (85.1%), of the anterior commissure, (82.6%), and the laryngeal surface of the epiglottis in (84.3%). Endoscopic techniques are a big advantage in modern surgery and diagnostic medicine. Their advancement in the last decades has opened new possibilities for the development of numerous min-

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imally invasive observations and surgical manipulations, resulting in minimal traumatism, faster patient recovery, and fewer postoperative complications.[6]

The rationale of the study is that after conducting this study we will be able to select only one better scope out of these scopes to be used on patients rather than using two different scopes in order to reduce examination time and patient discomfort.

MATERIAL AND METHODS

A randomized control trial was done at the department of Otorhinolaryngology, Head & Neck Surgery department, PIMS, Islamabad for a period of 6 months from 22nd May 2018 to 22nd Nov 2018. A total of 582 patients were included in the study, who were divided into two groups i.e. group A (291), who underwent 70^0 rigid endoscopy while group B (291) underwent 90^0 endoscopy. The sampling technique was non-probability purposive sampling. Patients between 18 and 60 years of age of both genders who were willing for examination, were included. Patients with the overhanging epiglottis increased body mass index, patients having exaggerated gag reflex, those having trismus/ laryngeal pathology were not comfortable with the procedure and were excluded. Parameters that were evaluated during the endoscopies of both groups included successful visualization of the subglottic area, anterior commissure, and the laryngeal surface of the epiglottis. Successful visualization was taken into account, the ability to obtain a recording of the full region of interest.

RESULTS

A total of 582 patients were included according to the inclusion criteria of the study. Patients were randomly divided into two equal groups. Patients in Group A under-went the procedure using 70^0 rigid telescopes and those in Group B underwent using 90^0 rigid telescopes. Statistics of the age (years) of patients were also calculated in terms of mean and standard deviation. The mean age (years) in the study was38.88+12.71, as shown in Table. I. Distribution of gender of patients was calculated in terms of frequency and percentage of male and female patients. There were 196 (67.4%) male and 95 (32.6%) female patients who presented in group A, whereas 245 (84.2%) male and 46 (15.8%) female patients presented in group B, as shown in Table. II. There were 267 (91.8%) and 251 (86.3%) patients in groups A and B respectively, who successfully visualized (subglottic area) was seen which was statistically significant (p-value 0.034), as shown in Table. III. Similarly, there were 261 (89.7%) and 239 (82.1%) patients among both the groups with successfully visualized anterior commissure which was statistically significant (p-value 0.009), as shown in Table. III Comparison of success rate among both the groups was assessed in terms of successfully visualized laryngeal surface of the epiglottis as 273 (93.8%) and 240 (82.5%) respectively, which was statistically significant (p-value 0.000), as shown in Table. III.

Table 1: Descriptive statistics of Age (years) of patients

Age in Years	Mean	SD +_
Total	38.88	12.71
Group A	39.21	12.94
Group B	38.56	12.48

Table 2: Distribution of Gender

Gender	Group A	Group B	Total
Male	196 (67.4%)	245 (84.2%)	441 (75.8%)
Female	95 (32.6%)	46 (15.8%)	141 (24.2%)
Total	291	291	582

Table 3: Comparison of Successful Visualization Hidden Areas of Larynx

Hidden Area	Group A	Group B	p-Value
Subglottis	267 (91.8%)	251 (86.3%)	0.034
Ant Commissure	261 (89.7%)	239 (82.1%)	0.009
Laryngeal surface of epiglottis	273 (93.8%)	240 (82.5%)	0.000

DISCUSSION

To evaluate laryngeal lesions indirect and fiber-optic laryngoscopy has a key role, but there are certain areas which are difficult to examine. Direct visualization and biopsy can be done by direct laryngoscopy but it is invasive, general anesthesia is needed and it depends on the surgeon's expertise. In addition to this, viewing is limited to the lumen and transmural evaluation is restricted, also the larynx has a complex anatomy and multiple regions such as ventricle, commissures, and subglottic areas, which are difficult to examin [8-11].

Various diagnostic radiological imaging methods e.g. CT and MRI are now available and it makes it possible to diagnose laryngeal lesions[12]. In otolaryngology outpatient clinics rigid endoscopes are used for examination of the larynx with some advantages, as the image is clear, large, and bright, which allows early diagnosis. Some patients are unable to tolerate rigid laryngoscopy, especially, those with a sensitive gag reflex, patients with limited jaw or neck mobility, or patients suffering from stridor. It can be performed with difficulties in infants and children[13-15].

Joachim Kettenbach et al.[16-21] demonstrated, that rigid endoscopes in high-risk patients have limited clinical application as the patient may require general anesthesia, while an experienced endoscopist and a cooperative patient both are required for successful examination by a flexible endoscope. The information which cannot be obtained by endoscopic laryngeal examination, cross-sectional imaging using spiral CT or MRI, and post-processing

of imaging data sets, may offer an additional evaluation tool. In our study, the mean age (years) in the study was 38.88+12.71. While another Study [9] it was found that the mean age was 36 years in their sample. In our study, there were 67.4% male and 32.6%[12]female patients presented in group A whereas 84.2% male and 15.8% female patients presented in group B. A study conducted by Raghebet al[9] enrolled 14 patients in the study group, 75% males and 25% females. In our study, the success rate of 70^0 and 90^0 rigid endoscope in successful visualization of the hidden areas of the larynx were 91.8% and 86.3% in patients it was successfully visualized (subglottic area) was seen among both the groups. Whereas another study conducted by Jun Shao, Jennifer Stem, Zheng-Min et al[7] provided a successfully visualized the subglottic area in patients i.e. 91.7% and 85.1% in both groups respectively. In our study, there were 89.7% and 82.1% patients among both the groups which were successfully visualized with anterior commissure. Whereas another study conducted by Jun Shao, Jennifer Stem, Zheng-Min et al[7] provided successful visualization of the anterior commissure in 92.6% and 82.6% of patients in both groups respectively. In our study, the comparison of success rate among both the groups was assessed in terms of successfully visualized laryngeal surface of the epiglottis as 93.8% and 82.5% in both groups. Whereas another study conducted by Jun Shao, Jennifer Stem, Zheng-Min et al[7] provided successful visualization of the laryngeal surface of the epiglottis in 94.2% and 84.3% of patients in both groups respectively.

CONCLUSION

The study findings concluded that the rate of 70^0 rigid endoscope was more successful in the visualization of the hidden areas of the larynx as compared to 90^0 rigid endoscope.

RECOMMENDATION

Further studies at multiple setups must be conducted to adopt a uniform protocol regarding the usage of one endoscope rather than using two different scopes, to reduce examination time and patient discomfort.

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Following authors have made substantial contributions to the manuscript as under

Junaid M:	Manuscript writing, concept, Study Design
Roohullah M:	Data collection
Din IU:	Manuscript writing, concept, Study Design
Hussain A:	Study design, overall supervision, and approval of the final version.
Khan MA:	Data collection, helping in manuscript writing

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

ORIGINAL ARTICLE

IMPACT OF FAMILIAL AND ENVIRONMENTAL RISK FACTORS ON AGE OF ONSET OF SCHIZOPHRENIA

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ABSTRACT

Objectives: To determines impact of familial risk factor i.e. positive family history of schizophrenia on age of onset of schizophrenia. 2. To determine impact of environmental risk factor i.e. substance misuse on age of onset of schizophrenia.

Materials and Methods: In this cross sectional analytical study, 430 patients were enrolled from Sarhad Hospital for Psychiatric Diseases Peshawar through convenience non probability sampling technique. First Data was dichotomized on the basis of positive and negative family history of schizophrenia and later on the basis of positive and negative history of substance misuse. Frequency and percentage were calculated for categorical variable while mean and standard deviation for continuous variables. Independent-samples T test was used to compare means of two independent variables.

Results: The mean age of onset of schizophrenia is 22.28 years with early onset in males than females. In those with familial schizophrenia, the mean ages of onset of schizophrenia in males and females are 22.35 and 22.05 years while in those with sporadic cases, the mean age of onset of schizophrenia in males and females are 21.83 and 25.43 years respectively. Moreover non-tobacco substances and cannabinoids are having statistically significant impact on age of onset of schizophrenia.

Conclusion: There is significant gender difference in age at onset of schizophrenia and substance misuse. Family history of schizophrenia eliminates the gender difference in age at onset of schizophrenia. Moreover non-tobacco substances and cannabinoids misuse can cause early onset of schizophrenia.

Keywords: Familial risk factor, Environmental risk factor, substance misuse, means age of onset of schizophrenia.

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INTRODUCTION

Schizophrenia is a lifelong major psychiatric illness with heterogeneous etiology characterized by positive and negative symptoms as well as behavioral disorganization and cognitive symptoms. About 0.3% to 0.7% of people are effected by schizophrenia worldwide during their life time[1]. The peak for age of onset of schizophrenia is between 20 to 35 years, with early onset in males by 3 to 4 years as compare to females. The incidence estimates among Male and females are 4.15 and 1.71 per 10,000 persons per year respectively[2,3]. The mean age of onset of schizophrenia is 21.44 years; 20.55 years for males and 22.67 years for females while mean age of onset of tobacco misuse is 17.2 years[4,5]. According to a systematic review the pooled estimate of the gender difference is of 1.07 years with males having earlier onset as compare to females[6]. The peak in age is equal for both genders at age of 22 with a difference in the mean age at onset being later for females[7]. Difference between males and female about age of onset of schizophrenia is only in sporadic cases and does not exist between those with familial schizophrenia or when there is comorbid cannabinoids misuse. Positive family history of schizophrenia, comorbid cannabinoids misuse and poor premorbid adjustment are associated with early onset of schizophrenia. Early onset schizophrenia is associated with poor clinical and social outcomes, larger cognitive deficit and less suicide rates as compare to late onset schizophrenia[2]. According to another study Genetic risk factors causes early onset of schizophrenia more in females than males, poor course of illness and increased risk of illness in siblings[7]. Late onset schizophrenia is associated with weaker family history of schizophrenia, decrease rates of comorbid substance misuse, higher educational attainment and better premorbid adjustment[8]. In short when genetic load is high the sex difference in age of onset of schizophrenia is smaller or abolished at all. Type of onset and core symptoms doesn't differ between , males and females[3,5].

Comorbid substance misuse is quiet common in patients with schizophrenia. Substance misuse causes poor prognosis, is an established fact. But its role in etiology is controversial[9]. In different studies the prevalence of substance misuse in schizophrenic patients varies from

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10% to 70% depending upon the type of population under study and different criteria and definitions used[10]. Positive family history of psychiatric disorders and lifetime cannabis use are significantly associated with earlier onset of schizophrenia in both males and females[11]. According to a meta-analysis, cannabis abuse can cause early onset of schizophrenia by at least 2.7 years. And this is evenly more significant when only female gender is considered[12,13]. According to a study, Substance misuse is more common in schizophrenia as compare to bipolar affective disorder. Cannabis misuse can cause early onset of schizophrenia and vice versa. Among cannabis user, mean ages of onset of schizophrenia and bipolar affective disorder were comparable. However among non-user, bipolar patients were older than schizophrenic patients regarding their age of onset of illness. Cannabis misuse unmasks pre-existing genetic liability that is partially shared between bipolar disorder and schizophrenia[14]. However tobacco smoking doesn't affect mean age of onset of schizophrenia[15]. Similar studies have been conducted at national and international level but no such study has been conducted in our set up i.e. that is Khyber pakhtunkhwa in near past. This study will highlight the role of substance misuse and family history of schizophrenia in age of onset of schizophrenia.

MATERIAL AND METHODS

In this cross sectional analytical study 430 patients were enrolled through nonprobability convenience method of sampling from Sarhad Hospital for Psychiatric Diseases Peshawar from October 2020 to march 2021. Any patient who met criteria of International Classification of Disease Research version 10 (ICD-10) for schizophrenia and gave a valid consent was included. Information was collected from patients, accompanied attendants and record and hospital record if any through questionnaire after confirming diagnosis by consultant. If there was any ambiguity regarding dates, circumstantial evidence was taken. Misuse (of substances) was defined per ICD10 criteria as maladaptive patterns of substance use that impair health in broad sense (physically, psychologically and or socially). And the pattern of use has persisted for at least one month or has occurred repeatedly within a twelve-month period.

In first step frequency and percentage were calculated for all categorical variables. In second step, mean for ages of onset of schizophrenia and substance misuse was calculated. In third step, patients were segregated into two groups based on positive and negative family history of schizophrenia. Later on each group was further dichotomized on the basis of gender. In fourth step, patients were segregated into two groups with positive and negative history of substances misuse. Similar groups were also formed for tobacco, non-tobacco substances and cannabinoids misuse. Independent-samples T test was used to compare means of two independent variables using SPSS version 24 for statistical analysis.

RESULTS

Out of 430 patients, 85.1% are males and 14.90% are females. The frequency and percentage of various categorical variables are given in table 1. The mean ages of onset of schizophrenia and substance misuse are given in table 2. There was statistically no significant difference (p= 0.983) in mean ages of onset of schizophrenia between those with positive and negative family history of schizophrenia. But when each group was further dichotomized into males and females then there was statistically significant difference (p= 0.002) in mean ages of onset of schizophrenia between males and females in those with negative family history of schizophrenia. Further detail is given in table 3. As shown in table 4, there was statistically significant difference in mean age of onset of schizophrenia only in between those, who were having positive or negative history of non-tobacco or cannabinoids misuse.

Table 1: Frequency and percent of different categorical variables

		Frequency	Percent
Gender	Male	366	85.10
	Female	64	14.90
Education	No education	222	51.60
	Primary education	26	06.00
	Middle education	56	13.00
	High education	67	15.60
	Higher education	59	13.70
Marital status	Unmarried	191	44.40
	Married	212	49.30
	Divorced	17	04.00
	Separated	10	02.30
Any family history of schizophrenia	Yes	132	34.60
	No	252	65.60
Substance misuse	Yes	300	69.80
	No	130	30.20
Tobacco misuse	Yes	294	68.40
	No	136	31.60
Non-Tobacco substances misuse	Yes	179	41.60
	No	251	58.40
Cannabinoids misuse	Yes	176	40.90
	No	254	59.10

Table 2: Mean of current age, age of onset of schizophrenia and substance misuse

Gender	Current/ Present age N=430	Age of onset of schizophrenia N=428	Age of onset of substance misuse N= 290
Male	33.82 ± 10.74	21.96 ± 5.97	17.96 ± 7.03
Female	34.12 ± 11.03	24.12 ± 8.07	19.45 ± 4.42
Total	33.86 ± 10.77	22.28 ± 6.36	18.01 ± 6.96

Table 3: Impact of family history of schizophrenia on mean age of onset of Schizophrenia

Any family History of schizophrenia N= 382	Gender	Mean age of onset of schizophrenia	Sig. (2-tailed)	95% Confidence Interval of the Difference
Yes		22.30 ± 6.35	0.983	-1.33 ± 1.36
No		22.32 ± 6.40		
Yes	Male	22.35 ± 5.98	0.849	-2.82 ± 3.43
	Female	22.05 ± 8.39		
No	Male	21.83 ± 5.96	0.002	-5.88 ± -1.30
	Female	25.43 ± 8.13		

Table 4: Impact of substance misuse on mean age of onset of schizophrenia

History of substance misuse N=428		Mean age of onset of schizophrenia	Sig. (2-tailed)	95%Confidence interval of the difference
Substance misuse	Yes	22.23 ±5.99	0.777	-1.50±1.12
	No	22.42 ±7.17		
Tobacco misuse	Yes	22.23 ±6.03	0.788	-1.47 ± 1.12
	No	22.41 ±7.05		
Non-Tobacco substances misuse	Yes	21.50 ±5.43	0.032	-2.56 ± -0.117
	No	22.84 ±6.91		
Cannabinoids Misuse	Yes	21.55 ± 5.45	0.047	-2.47 ± -0.015
	No	22.79 ±6.89		

DISCUSSION

Age of onset of schizophrenia: In this study the mean age of onset of schizophrenia is 22.28 ± 6.36 years: 21.96 ± 5.97 years for males and 24.12 ± 8.07 years for females. So onset of schizophrenia is almost 2.1 years later in females as compare to males. These findings supported the findings of Miettunen et al[2]. The late onset in females may be due to protective role of female sex hormones. Frequency and age of onset of substance misuse: In our study the frequency of any substance misuse is 69.80%: 68.40% for tobacco, 41.60% for non-tobacco substances and 40.90% for cannabinoids. This is according to the work of Winklbaur and Mallet.J[4,10]. The increase frequency of substance misuse among schizophrenic patients is due to their shared genetic vulnerability, negative symptoms of schizophrenia and side effects of medications[16,17]. The mean age of onset of substance misuse is 18.01 ± 6.96 years: 17.96 ± 7.03 years for males and 19.45 ± 4.42 years for females. So onset of substance misuse precedes onset of schizophrenia in our study. Moreover onset of substance misuse is almost 1.49 years earlier in males as compare to females. This is contradictory to the study of Naqvi at el[18].

Impact of familial risk factor i.e. positive family history of schizophrenia on age of onset of schizophrenia: In our study the mean ages of onset of schizophrenia in those with positive and negative family history of schizophrenia are 22.30 ± 6.35 years and 22.32 ± 6.40 years respectively. So there was no statistically significance difference (p=0.98) between the two groups when gender is ignored. However when each group is further dichotomized on the basis of gender then statistically significant difference arises (p= 0.002) between males and females with in group of negative family history of schizophrenia: 21.83 ± 5.96 years for males and 25.43 ± 8.13 years for females (age of onset of schizophrenia). These findings support our hypothesis that Positive family history of schizophrenia or more genetic load minimizes or eliminates the gender difference in mean age of onset of schizophrenia. These findings are consistent also with work of Hare and Dassori, in which they looked at the heritability of age of onset of psychosis in schizophrenia in 2010[5]. In their study too when genetic load is high the difference in mean age of onset of schizophrenia between males and females is abolished.

Impact of environmental risk factor i.e. substance misuse on age of onset of schizophrenia: Substance misuse can affect mean age of onset of schizophrenia and the evidence is more in favor of cannabinoids as compare to other substances[11]. Keeping in view table No.4, there is statistically no significant difference in mean age of onset of schizophrenia when tobacco (p=0.788) and any substance misuse (p=0.777) are dichotomized into “Yes” and “No” groups. These findings are also consistent with work of Hickling and Ayesha[15]. Statistically significant difference in mean age of onset of schizophrenia is produced when non-tobacco misuse (p=0.032) and cannabinoids misuse (p=0.047) are dichotomized into “Yes” and “No” groups. For non-tobacco substance misuse, the mean ages of onset of schizophrenia are 21.50 ± 5.43 years for “Yes” group and 22.84 ± 6.91 years for “No” group. The onset is 1.3 years earlier in those who are misusing non-tobacco substances. For cannabinoids misuse, the mean ages of onset of schizophrenia are 21.55 ± 5.45 years for “Yes” group and 22.79 ± 6.89 year for “No” group. So the onset of schizophrenia is 1.24 years earlier in those who are misusing cannabinoids. Compton and Kelly also concluded similarly in their study in 2009[13]. Even though much work

has been done in this regard but still there arises need to look at other contributory factors in mean age of onset of schizophrenia for example: 1. Quantification of genetic load regarding their impact on mean age of onset of schizophrenia; 2. Impact of other substances individually e.g. stimulants, opioids, alcohol, sedative hypnotics, volatile solvents and hallucinogens etc. on mean age of onset of schizophrenia.

Patients and attendants were asked retrospectively regarding age of onset of schizophrenia and substance misuse. So recall bias may be there. 2. No biochemical (urine/blood screening for illicit drugs) test was done to confirm or exclude presently/currently misuse of any substance.

Mostly patients with chronic and severe schizophrenia or those who are very poor to get free medicines are visiting Sarhad Hospital for Psychiatric Diseases Peshawar. So findings of these patients can't be generalized to all schizophrenic patients within community.

CONCLUSION

There is significant gender difference in age at onset of schizophrenia and substance misuse. Family history of schizophrenia eliminates the gender difference in age at onset of schizophrenia. Moreover non-tobacco substance and cannabinoids misuse can cause early onset of schizophrenia.

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AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under

Shakeel M:	Concept, study design, Confirming Diagnosis, Data collection and analysis, manuscript writing
Adeela:	Data collection, entry and analysis
Ali A:	Data collection
Khan T:	Establishing provisional diagnosis

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

ORIGINAL ARTICLE

COMPARISON OF THE ROLE OF EARLY VERSUS DELAYED FIXATION OF INTRACAPSULAR FEMORAL NECK FRACTURE IN YOUNG POPULATION IN TERMS OF AVASCULAR NECROSIS OF THE FEMORAL HEAD

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ABSTRACT

Objective: To compare the role of early versus delayed fixation of intracapsular fracture of the femoral neck in young population in terms of Avascular Necrosis (AVN) of Femoral Head.

Material and Methods: This quasi-experimental study was conducted in Peshawar from January 2020 till June 2021 at the Khyber Teaching hospital and all patients with age 18 to 60 years who had the neck of femur fracture were included who presented within one week of fracture. Group 1 consisted of the early fixation group (fixated within 24 hours) while group 2 consisted of the late fixation group (those who fixated after 24 hours). The development of AVN was assessed on follow-up X-ray at 6 weeks, 3 months, and 6 months. Data was analyzed using SPSS. Mean and standard deviation was used for quantitative data. Frequency and percentages were used for qualitative data. A p-value of ≤ 0.05 was taken as significant. Shapiro Wilk's test was done to find the normality of the data.

Results: The mean age of the 64 included patients was 52 ± 5 years. The male to female ratio was 1:1.5. A total of 34 patients belonged to group 2 while 30 to group 1. In group 2, 11 patients experienced osteonecrosis of the femoral head. While in group 1, 9 patients experienced osteonecrosis of the femoral head. No significant effect of time delay on the chances of developing osteonecrosis of the femoral head was noted in group 2 even after a delay of 24 hours with a p-value of 0.201.

Conclusion: We conclude that there is no significant difference in the outcome of femoral neck fractures whether it was fixed early or late.

Key Words: Neck of femur fracture, Garden classification, Avascular necrosis of the femoral head.

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INTRODUCTION

Fractures of the neck of the femur can be described as the current "Orthopedic epidemic" due to its large number of emergencies in orthopedic wards[1]. Younger patients have a small proportion of these fractures i.e. up to 3% of all hip fractures[2]. In aged patients, the preferred method of treatment is hip replacement, either hemiarthroplasty or total hip replacement[3]. In young patients, under 60 years of age, the heads are being preserved, by early fracture fixation as the treatment of choice[4, 5]. Avascular necrosis (AVN) of the femoral head and non-union of the neck of the femur are the common complications of fractures fixation, but it also includes other complications i.e. neurovascular compromise, osteoarthritis of the hip, limb shorting, varus or valgus deformity of the femoral head, deep vein thrombosis and wound infection can also occur[6]. In patients under 60 years of age, the fractures are less common and we don't have much evidence to support any treatment method[4, 5]. In younger patients, the head should be preserved and hip replacement should be the last option, keeping in

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view their increased level of activities[7]. Furthermore, there are increased chances of complications of fractures at the neck of femur fixation, especially non-union and (AVN) of the femoral head i.e. 35% and 45% respectively [4, 8, 9]. Currently, in literature, there are conflicting views regarding the ideal time of fractures fixation. This study aims to compare the role of early and delayed fixation in femoral neck fracture in the young population about AVN.

MATERIAL AND METHODS

This quasi-experimental study on 64 patients was conducted in the Khyber teaching hospital from January 2020 till June 2021. The inclusion criteria were patients from 18 to 60 years of age presenting up to 1 week of neck of femur fracture. The exclusion criteria was open and pathological fractures or ipsilateral fracture neck and shaft of the femur. The patients were non-randomly divided based on their time of arrival after the initial injury to the time of fixation. The early group with a history of the initial trauma and time of fixation within 24 hours and the late group with the history of initial trauma and time of fixation more than 24 hours. The method of fixation was 2 or 3 cannulated screws depending on the neck size, under image intensifier on a fracture table, through lateral approach after close or open reduction under spinal or general anesthesia. The follow-up protocol was 6 weeks, 3 months, and 6 months in which the (AVN) of the femoral head was diagnosed by X-ray anteroposterior and lateral view and clinically. The time of fixation was correlated with the occurrence of AVN of the femoral head using SPSS.

RESULTS

A total of 64 patients were included with ages ranging from 18-60 and a mean of 52 ± 5 years. The basic demographics of the study are discussed in table 1. A total of 34 patients were included in group 2 while 30 to the group 1. Eleven patients of group 2 experienced AVN of the femoral head. While in group 1, 9 experienced osteonecrosis of the femoral head. The chances of developing osteonecrosis of the femoral head were not significantly related to time delay and a p-value of 0.201 was calculated using the chi-square test as discussed in Table 2.

Table 1: Basic Demographics of the Study

Frequencies and percentages for age		
Age Groups	Frequencies	Percentages
18-30 years	12	18.75%
31-40 years	13	20.31%
41-50 years	21	32.81%
51-60 years	18	28.12%
Mean and SD for Age		52 ± 5 years
Frequencies and percentages for gender		
Gender Groups	Frequencies	Percentages
Male	21	32.81%
Female	43	67.19%
Male to Female Ratio		1:2
Frequencies and percentages developing AVN		
Avn Status	Frequencies	Percentages
Present	20	31%
Absent	44	69%

Table 2: Comparison between early and late fixation group

Chance of developing AVN between early and late fixation group		
Fixation time	Frequencies of developing AVN	P-value (Chi-square)
Early Group 1	9	0.385
Late Group 2	11	0.201

DISCUSSION

AVN of the femoral head is an unpredictable and serious complication developed after the displaced intracapsular neck of femur fractures. Due to disruption in the blood supply of the femoral head. And it is also thought that AVN of the femoral head is more common in the neck of the femur fractures with delayed time of fixation, in patients under 60 years of age i.e. 16% to 86% [4, 8-11]. In younger patients, there is a high incidence of non-union and AVN of the femoral head [9, 11]. The AVN of the femoral head can lead to the collapse of the femoral head followed by osteoarthritis which then needs other surgical procedures [12]. In literature, the union rate in the neck of femur fractures is 70% and a failure rate is 30% in young patients. It means the initial trauma which leads to displacement of fracture is the main reason for the disruption of vascular supply to the femoral head and followed by osteonecrosis of the femoral head. The time duration from injury to fixation of neck of femur fractures is usually considered as an important factor[13] but there is no clear evidence of complications between the time of injury to fixation, as reported in other series[8, 11, 14]. Probably it is the severity of trauma at the time of initial injury which leads to damage to the blood supply of the femoral head and early reduction and fixation having no effect on this and its complications. For example, Jain et al concluded that there are high chances of postoperative complications with fracture fixation done after 12 hours of injury [15], while Karaeminogullari et al, encountered no difference between time to fixation and (AVN) of the femoral head[16]. In our studies, we found that the time to fixation of neck of femur fracture had no significant

role in the development of AVN of the femoral head.

In fracture neck of the femur, the degree of displacement is the main risk factor leading to a high risk of (AVN) of the femoral head. Gerber et al have noted that urgent open reduction and fixation will not prevent (AVN) of the femoral head in displaced fractures and they didn't recommend the immediate aspiration or decompression and fixation, because the results were the same whether to be operated on day 1 or after 2 days [17]. Anatomical reduction and stable internal fixation of fractures of the neck of the femur decrease the chances of AVN of the femoral head and therefore it is considered as standard goal of therapy. There is no association between delay time to fixation and AVN of the femoral head in young patients[12]. In another study by Karaeminogullari et al, there is no difference in the frequency of AVN of the femoral head and nonunion rates in the neck of femur fractures in patients who were fixed before or after 12 hours of injury[16] which also coincides with our study. This study also shows AVN of the femoral head and nonunion were 15.5 % and 25 % before 12 hours after injury vs 14% and 27% after 12 hours of injury[16] which is consistance with our study. In another study, there was no difference in frequency of osteonecrosis of femoral head fixed either before or after 24 hours of injury 25% and 20% respectively[8]. Upadhyay et al also found no difference in osteonecrosis of femoral head or malunion in patients even fixed after 48 hours of injury[11]. We suggest that fixation of femoral neck fracture can be fixed even up to more than 24 hours after encountering the initial trauma with no significant chances of developing AVN.

CONCLUSION

Our study concludes that there is no significant difference in the outcome of femoral neck fractures whether it was fixed early or late. Delay in treatment i.e., fixation of the femoral head after the initial trauma has been found to have no significant role in AVN of femoral neck fracture and the fixation can be delayed up to more than 24 hours with no significant chances of developing AVN of the femoral head.

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Following authors have made substantial contributions to the manuscript as under

Khan MS:	Concept/ Idea, Literature, review, Drafting & Final Review
Khan MY:	Concept/ Idea, Analysis & Interpretation of Data, References
Sajjad A:	Manuscript Writing, Literature review, Analysis & Interpretation of Data
Ullah H:	Concept/idea, Data Collection
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Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

ORIGINAL ARTICLE

IMMUNOHISTOCHEMICAL EXPRESSION OF P53 IN ORAL SQUAMOUS CELL CARCINOMA, ORAL EPITHELIAL PRECURSOR LESIONS, AND NORMAL ORAL MUCOSA

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ABSTRACT

Objective: To assess the immunohistochemical expression of p53 in tissue samples of oral squamous cell carcinoma (OSCC), oral epithelial precursor lesions, and normal oral mucosa.

Material & Methods: A comparative cross-sectional study was jointly conducted at the Departments of Pathology and Oral and Maxillofacial Surgery of various medical and dental institutes of the country from April 2016 to March 2017. A total of 180 subjects were included in the study. Oral tissue specimens were collected for laboratory investigations after obtaining written consent from all subjects. p53 was assessed using immunohistochemistry in tissue samples of 60 cases of OSCC, 60 cases of epithelial precursor lesions, and normal oral mucosal samples of 60 healthy individuals. Data were recorded, evaluated, and analyzed by SPSS-20.

Results: p53 protein expression was noted in 85% OSCC and 73% oral epithelial precursor lesions. Among healthy individuals, one subject showed p53 immunoreactivity in the normal oral mucosa.

Conclusion: Raised p53 overexpression in OSCC and oral precursor lesions, compared to normal oral mucosa make it a probable candidate for a potential predictive biomarker in oral premalignancy and malignancy.

Keywords: Oral squamous cell carcinoma, Tumor suppressor protein p53, Immunohistochemistry.

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INTRODUCTION

Oral cancer represents a remarkable component of global cancer burden, with raised morbidity and mortality.[1] According to the collective cancer registry report of Shaukat Khanum Memorial Cancer Hospital and Research Centre, Lahore, Pakistan, from December 1994 to December 2019, the carcinomas of lip and oral cavity is marked as the 3rd most frequently occurring malignant tumor in Pakistan.[2] OSCC is the commonly occurring histopathological variant of oral epithelial malignancy.[3] Frequently, it is anteceded by epithelial precursor lesions. The epithelial precursor lesions are characterized histopathologically as squamous cell hyperplasia with or without other specific cytological and architectural alterations termed as oral epithelial dysplasia (OED), subcategorized as mild, moderate, severe; dysplasia and carcinoma in situ. [4]

OSCC are usually marked by late-stage diagnosis and low survival rates and epithelial precursor lesions are characterized by varied risk of malignant transformation.[3,4] Thus improving the prognosis, researchers are consistently searching for biomarkers that can have a predictive role in clinical practice related to oral malignancy and premalignancy.[5] One of the key events noted in the multistep process of development of oral malignancy and premalignancy is the inactivation of tumor suppres-

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sor genes (TSGs).[6-10] p53 is the most immensely explored gene among the TSGs, linked with oral cancers and associated oral potentially malignant precursors.[9,10] p53 role is noteworthy as in the research literature, it has been titled as "molecule of the year", the guardian of genome & policeman of oncogenes.[11] Epidemiological studies have noted the alterations in p53 gene, leading to accumulation of p53 protein in the tissue samples of oral cancerous and precancerous lesions.[10,12,13,14] In the present study, p53 immunohistochemical status was evaluated among cases of OSCC, OPMDs and healthy individuals to inquire into its clinical usefulness.

MATERIAL & METHODS

The present descriptive cross-sectional study was carried out after approval from the Institutional review board and permissions from the head of the oral and maxillofacial surgical units of Peshawar Dental College (PDC), Khyber college of dentistry (KCD) & PIMS, and head of the histopathology department PIMS, from 3rd April 2016 to 31st March 2017, by adopting a non-probability and purposive sampling technique. The study was conducted on the tissue samples of 180 subjects comprising 60 cases of OSCC (Group A), 60 cases of epithelial precursor lesions (Group B), and 60 healthy individuals (Group C). A detailed history of the study participants was recorded on a structured proforma. Both tobacco users and non-users were part of the study and tobacco usage history was recorded for all the participants (i.e., tobacco usage [Present, Ex, Non-user], type of tobacco products (Smoked tobacco [ST], Smokeless tobacco [SLT], duration of tobacco use in years and daily frequency of tobacco usage). The inclusion criteria for group A includes histopathologically diagnosed cases of OSCC, while for group B includes those oral mucosal biopsies which were characterized by oral epithelial hyperplasia with or without dysplasia and carcinoma in situ. Normal oral mucosa was collected from healthy individuals. The healthy individuals were those who consented to the study participants and visited the recruited centers for dental treatments comprising of 3rd molar surgical extractions, alveoloplasty, etc., in which an extra portion of normal oral mucosal tissue was removed and intended to be discarded due to need of the procedure. [15] The oral mucosal tissues were processed and stained by hematoxylin and eosin for histopathological slide review. The H&E staining confirmed the diagnosis of OSCC and oral epithelial precursor lesions in the tissue samples, while the p53 staining was evaluated by immunohistochemistry by a semi-quantitative scoring system. Special grip-coated slides (Dako Flex IHC Microscope slides) were used for immunohistochemical staining of the tissue samples of the study participants with p53 protein antibody (Clone: DO-7; Antibody type: Monoclonal mouse, Dako, Denmark). The protocol employed for scoring p53 immunoreactivity consists of marking the OSCC and oral epithelial precursor lesion specimen slides either positive or negative. The basic criteria for positive stain were the presence of clear brown nuclear stain. The percentage of stained nuclei was assessed by enumerating p53 stained cells per 100 anaplastic, hyperplastic or dysplastic epithelial cells in the area of best staining with the cut-off value of 10% nuclei stained with p53 immunohistochemically. The p53 stained nuclei counts were categorized into the following 4 categories; absence of the stain or occasional keratinocytes staining (-), staining of 10-33% of keratinocytes (+), staining of 34-66% of keratinocytes (++), staining of greater than 66% of keratinocytes (+++). The intensity of the stain was subjectively graded into the definite but light stain (1+), darker stain (2+), and most intense stain(3+).[12,13] In the tissue sections of the normal oral mucosa, p53 stained nuclei counts were categorized into the following two categories; the negative stain comprise of the absence of expression of p53 protein detected in any epithelial nuclei or even rare cells positive (1-10 cells per section), while the positive p53 immunohistochemical stain was marked when clear brown colored staining with more than 5% of suprabasal cells showed positivity.[14,16,17] In epithelial tissue specimens of oral epithelial precursor lesions and healthy individuals, p53 staining confined exclusively to basal layers only was considered normal expression and marked as a negative case. International Federation of Gynecology and Obstetrics (FIGO) grade 3 endometrioid carcinoma was employed as a positive control for the p53 immunoreactivity.

The data obtained were analyzed by using SPSS version 20. The percentages were calculated for each categorical variable and a Chi-square test was applied for statistical significance, where appropriate. A probability value of less than and equal to 0.05 was considered statistically significant.

RESULTS

The results of our study are summarized in Tables 1-3. The observed mean age of cases of OSCC, epithelial precursor lesions, and healthy individuals was 55 (SD-14.43), 54.5 (SD-14.41), and 50 (SD-11.83) years, respectively.

p53 immunoreactivity was observed in 51(85%) out of 60 lesions of OSCC and 44 (73.3%) out of 60 cases of epithelial precursor lesions. In the normal oral mucosa of healthy individuals, out of sixty samples, only one (1.7%) showed suprabasal staining of p53 protein. A statistically significant difference was recorded among the study participants for p53 immunohistochemical level, staining intensity, and p53 immunoreactivity in tissue specimens of OSCC and OPMD lesions and normal oral mucosa (Table-1).

Among OSCC cases, most of the lesions were WDSCC (46.7%) and among epithelial precursor lesions, most of the lesions presented as squamous cell hyper-

Table 1: p53 immunohistochemical staining level in tissue specimen of the study participants

A) Level of p53 immunohistochemical stain	***OSCC lesions***	***Epithelial precursor lesions***	***Normal oral mucosa of healthy individuals***	***Total***	***p-value***
Absence or occasional keratinocyte staining (-)	9 (15%)	16 (26.7%)	59 (98.3%)	84(46.7%)	<0.01*
Staining of 10-33% of keratinocytes (+)/ Supra basal staining in normal oral mucosa	27 (45%)	40 (66.7%)	1 (1.7%)	68 (37.8%)	
Staining of 33-66% of keratinocytes (++)	10 (16.7%)	4 (6.7%)	-	14 (7.8%)	
Staining of greater than 66% of keratinocytes (+++)	14 (23.3%)	-	-	14 (7.8%)	
B) Staining intensity of p53	***OSCC lesions***	***Epithelial pre-cursor lesions***	***Normal oral mucosa of healthy individuals***	***Total***	***p-value***
					<0.01*
None	9 (15%)	16 (26.7%)	59 (98.3%)	84 (46.7%)	
Definite but light stain (1+)	24 (40%)	20 (33.3%)	1 (1.7%)	45 (25%)	
Darker stain (2+)	23 (38.3%)	19 (31.7%)	-	42 (23.3%)	
Most intense stain (3+)	4 (6.7%)	5 (8.3%)	-	9 (5%)	
C)Tissue p53 Immunoreactivity	***OSCC lesions***	***Epithelial pre-cursor lesions***	***Normal oral mucosa of healthy individuals***	***Total***	***p-value***
Positive	51 (85%)	44 (73.3%)	1 (1.7%)	96 (53.3%)	<0.01*
Negative	9 (15%)	16 (26.6%)	59 (98.3%)	84 (46.6%)	
Total	60 (100%)	60 (100%)	60 (100%)	180 (100%)	

*Pearson's Chi-square test

Table 2: p53 immunoreactivity and histopathological parameters of OSCC and epithelial precursor lesions

Histopathological Features	**Tissue p53 immunoreactivity**		**Total**	**p-value (Chi-square Test)**
	Negative	Positive		
WHO Grading System of OSCC				
Well Differentiated SCC	3(5%)	25(41.7%)	28(46.7%)	0.683*
Moderately Differentiated SCC	5(8.3%)	22(36.7%)	27(45%)	
Poorly Differentiated SCC	1(1.7%)	4(6.7%)	5(8.3%)	
Epithelial precursor lesions				
Squamous cell hyperplasia	8(13.3%)	29(48.3%)	37(61.7%)	0.113*
Mild dysplasia	4(6.7%)	6(10%)	10(16.7%)	
Moderate dysplasia	2(3.3%)	8(13.3%)	10(16.7%)	
Severe dysplasia	-	1(1.7%)	1(1.7%)	
CIS	2(12.5%)	-	2(3.3%)	

*Pearson's Chi-square test

Table 3: Relation between tissue p53 immunoreactivity and age, gender & Tobacco usage (p-value)

Variables	**OSCC**	**OPMDs**	**Healthy Individual**
Age in years >50 <50	0.85b	0.77a	1.0b
Gender Male Female	1.0b	0.21b	0.34b
Tobacco usage Tobacco user Ex tobacco user Non-tobacco user	0.56a	0.27a	0.24b

Type of Tobacco product Smoked tobacco (ST) Smokeless tobacco (SLT) Both ST & SLT	0.29a	0.31a	0.53a
Frequency of tobacco use per day 10-1 times/day >10times/day	0.06b	0.44a	0.06b
Duration of tobacco use in years 10-1 years 20-11 years >20 years	0.38a	0.13a	0.19b

a= Pearson's Chi-square test; b= Fisher's exact test

plasia (N=37/60;61.7%). Statistically, an insignificant difference was observed between p53 immunoreactivity and the WHO histopathological grading system among OSCC and epithelial precursor lesions (Table-2).

Among cases with OSCC lesions, statistically insignificant differences were observed between p53 immunoreactivity status and age, gender, tobacco usage status, type of tobacco product consumed, frequency of tobacco use per day, and in years (Table-3).

Among healthy individuals, out of 60 tissue specimens of the normal oral mucosa, only one (1.7%) sample showed suprabasal staining of p53 protein (Table-1).

DISCUSSION

Oral squamous cell carcinoma (OSCC) is the frequently occurring oral epithelial malignancy that mostly originates from oral potentially malignant disorders. [4] There is always a perpetual search for a biomarker that can assist in the timely prediction of malignant transformation of epithelial precursor lesions for improving the prognosis of OSCC.[5] In the present study, tissue p53 immunoreactivity was assessed in OSCC and epithelial precursor lesions with taking in consideration the normal oral mucosa to unfold its possible predictive role in the timely indication of oral malignancy and premalignancy.

The present study reported that most of the patients with OSCC and epithelial precursor lesions presented in the same mean age of 50±years as reported by other researchers.[3,18,19] Old age preponderance among cases of oral malignant and premalignant lesions is in obedience with the observations noted by other researchers also, who have marked age as a fear factor in OSCC development and foretelling index in potentially malignant epithelial precursors.[20-22]

In the present study, the highest frequency of tissue p53 immunoreactivity was noted among lesions of OSCC (85%) followed by epithelial precursor lesions (73%) compared to the normal oral mucosa (1.7%).

The observation of the highest percentage of p53 tissue expression among lesions of OSCC is comparable to studies in the region that reported p53 immunoexpression in a varied range. Ara et al., Hashmi et al., and Ghanghoria et al. reported tissue p53 phosphoprotein expression with a frequency of 67%, 66.1%, 63% and 54%.[23,18,24,25]

The difference in p53 protein expression may be due to the difference in p53 antibody clone used or regional risk habits related to OSCC lesions development.[8,25]

The present study observed a statistically significant relation between p53 staining intensity and p53 protein expression in tissue samples of OSCC. These findings are in obedience with the findings noted by Ara et al., and Azizi et al.,[23,26]

Among OSCC lesions, a statistically insignificant relation was observed between tissue p53 immunoreactivity and WHO OSCC grading system, age, gender, tobacco usage history, type of tobacco product consumed frequency of tobacco use per day, and duration of tobacco use in years. These findings are in obedience with the observations reported by Bhattacharya et al. [27] However, a study done by Gatto et al., revealed a statistically significant relation between p53 immunoreactivity and histological grades and tobacco and betel quid habits and insignificant relation with age, gender of OSCC lesion.[28]

The present study noted that among epithelial precursor lesions, 73.3% (N=44/60) showed tissue p53 immunoreactivity. This finding is comparable to the reported frequency of p53 immunoexpression in local and international studies.[21,29,30]

The present study recorded a statistically significant (p=<0.01) relation between p53 staining intensity in tissue and p53 expression among cases with epithelial precursor lesions, contrary to the study by Nagata et al., who reported a statistically insignificant difference between p53 staining intensity and p53 expression among cases of oral epithelial precursors.[31]

The present study noted an insignificant relation of p53 immunoreactivity with age, gender, tobacco usage history, type of tobacco product consumed, frequency of tobacco use per day, and duration of tobacco use in years, among cases with oral epithelial precursor lesions. These findings are consistent with a study conducted by Nagata et al., 2018; who recorded a statistically insignificant relation between p53 immunoreactivity and age and gender.[31]

Among healthy individuals, regarding normal oral mucosa, the present study revealed that only one subject

expressed p53 immuno-staining in suprabasal layers. These findings are contrary to other studies that observed that p53 protein expression was exclusively absent in all oral epithelial layers or present in the basal layer only but not noted in the suprabasal layers.[28,29]

Detection of p53 protein in normal oral mucosa is mostly absent due to the brief half-life of the wild type of p53 protein or due to expression of minimal quantity, which is difficult to be detected on immunohistochemistry.[32] The possible explanation for the collection of wild type of p53 phosphoprotein is that it might be an outcome of the defect in the degradation pathway or binding of wild type proteins to other proteins leading to the gathering of stabilized normal proteins or nonfunctional p53 phosphoproteins or probably as a physiological response of cells to the genotoxic stress.[19, 24] Among healthy individuals, the present study observed that p53 immunoreactivity was not significantly related to the age, gender, tobacco use status, type of tobacco products, tobacco use frequency per day, and duration of tobacco use in years.

CONCLUSION

The present study observed an increase in p53 protein expression in OSCC as compared to oral precursor lesions and decreased expression in the normal oral mucosa. Thus, concluding that p53 immunoreactivity can probably predict the susceptibility of potentially malignant tissue to transform into oral malignancy.

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AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under

Khan AS:	Concept/ Idea, Literature, review, Drafting & Final Review
Ahmed S:	Concept/ Idea, Analysis & Interpretation of Data, References
Iqbal F:	Analysis & Interpretation of Data
Saboor A:	Manuscript Writing, Literature review, Analysis & Interpretation of Data
Nisar M:	Concept/Idea, Data Collection
Nausheen T:	Concept/Idea, Literature review, Drafting & Final Review
Sheikh A:	Concept/Idea, Literature review
Haq M:	Concept/Idea, Literature review
Ahmed T:	Concept/Idea, Literature review, Drafting & Final Review
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Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

ORIGINAL ARTICLE

FREQUENCY OF SELF REPORTED ALLERGIC REACTIONS TO THE DRUGS AMONG MEDICAL STUDENTS OF PESHAWAR

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ABSTRACT

Objective: To determine the frequency of self reported drug induced allergic reactions among medical students of Peshawar.

Materials and Methods: A cross-sectional study was conducted on 300 students from various public and private sector medical colleges of Peshawar from Sept 2020 to June 2021. After a brief introduction and explaining the purpose of this study, a close-ended self-reported questionnaire was distributed among them. The questionnaire was comprised of demographic data, family history of atopic disease, source of drug allergy, signs and symptoms of allergy, and route of drug administration.

Results: Among 300 students, 23 participants indicated drug allergy with a self-reported frequency of 7.67%. The most frequently implicated drugs were antibiotics (52.17%), of which levofloxacin was the most common antibiotic followed by NSAIDs (17.39%). The most commonly reported allergic manifestations were cutaneous (34.8%), followed by gastrointestinal (17.4%) and respiratory (13.4%) symptoms. Of total allergic cases, 78% subjects had taken the drug in oral dosage form.

Conclusion: Self-reported allergic reactions to the drugs were highly prevalent with antibiotics as the most common source and cutaneous manifestations as the most common sign of drug allergy.

KEYWORDS: Drug allergy, Drug hypersensitivity, Self-reported, Prevalence

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INTRODUCTION

According to World Health Organization, adverse drug reaction (ADR) is an unintended, unwanted, and noxious response to a drug at doses used therapeutically in humans.[1] They occur in a small portion of population but not rare; with the documented incidence of 10-25% in different clinical settings. One of the unpredictable and dose-independent types of ADR is drug allergy or drug hypersensitivity, comprising 15% of all adverse drug reactions, generally serious, and requires drug withdrawal.[2]

In 2003, World Allergy Organization (WAO) defined drug allergy as an immunologically mediated drug hypersensitivity reaction. The mechanism of drug allergy or hypersensitivity could be either IgE or non-IgE mediated, with T-cell mediated reactions largely present in the later and producing stereotype symptoms that are unrelated to the pharmacodynamic profile of the drug.[3] They may occur even with much smaller doses and severity ranging from mild clinical manifestations like skin rashes to life-threatening conditions i.e. anaphylactic shock, serum sickness, Steven-Johnson syndrome and hemolytic anemia, etc. The target organs primarily affected by drug allergy are skin, airways, gastrointestinal tract, blood vessels, and blood.[4] This highlights the clinical significance of drug allergic reactions, which may prolong the duration of hospital stay, affect drug prescribing patterns of physicians and increase the socio-economic cost.

Several prospective studies evaluated the prevalence of ADRs but mostly they are type A reactions, so did not account for the drug allergy or hypersensitivity which is type B reaction.[5-7] There are few studies on the prevalence of drug hypersensitivity reactions in the general population where it is estimated that approximately 3-4% of children and more than 7% of the adult population experience a drug hypersensitivity reaction.[8-10] Moreover, surveys had been conducted in different parts of the world like Turkey,

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Portugal, UAE, and Brazil revealing some data on the epidemiology of drug-induced allergic reactions ranging from 5-25% of the population studied.[11-15] In our country, data related to ADRs is scarce and most of the available reports are limited to specific ADRs targeting only hospitalized patients. To the best of our knowledge, currently, there is no local data available regarding the frequency of allergic reactions to commonly used drugs in this region. This study was an attempt to explore it which will help us analyze the magnitude of the problem and identify common drugs causing hypersensitivity reactions in our local population. The target population was medical students considering their educational background that would help us deduce more reliable results.

MATERIALS AND METHODS

A multi-centered cross-sectional study was conducted from Sept 2020 to June 2021 for which a sample size of 300 subjects was calculated by Raosoft's sample size calculator using a 5% margin of error and 95% confidence level. After taking ethical approval from the institutional research committee, undergraduate students from various public and private sector medical colleges of Peshawar were enrolled in the study (irrespective of age, gender, economic status, and ethnic background). Non-probability, convenient sampling technique was used for the selection of participants. Each participant was informed about the study aspects in detail followed by their verbal consent. A well-structured close-ended questionnaire was distributed among students comprising of data regarding demographics, family history about the allergy, and personal experience of drug allergy. Participants who answered "YES" to the question were further asked to complete the remaining questions in the questionnaire like the type of drug involved, its dosage form, signs and symptoms of drug allergy.

The collected data was analyzed and transformed into appropriate graphs and tables using an excel sheet and SPSS version 22. Numeric values were expressed as Mean ± SD whereas the frequency of affirmative answers to each question was analyzed in percentages.

RESULTS

In this cross-sectional study, a total of 300 students from various medical colleges were enrolled having a mean age of 22.83 ± 1.9 years. 195 (65%) males and 105 (35%) females responded to the questionnaire. Among studied participants, 23 (7.67%) reported the incidence of drug allergy (Figure 1) of which 18 (78.2%) were male and 05 (21.7%) were female. 06 (26%) subjects revealed a positive history of drug allergy in the family.

As shown in Figure 2, 12/23 (52.17%) allergic participants indicated antibiotics as their source of allergy followed by NSAIDs/painkillers i.e. 4/23 (17.39%). A lower frequency of 1/23 (4.35%) was observed each with amitriptyline, carbamazepine, and alprazolam. Few participants i.e. 4/23 (17.39%) indicated more than one drug as a source of allergy. Among antibiotics, the highest frequency of 4/12 (33.3%) was observed with levofloxacin followed by moxifloxacin 3/12 (25%) and co-amoxiclav. Table 1 shows the distribution of clinical manifestations of drug allergy in different categories where majority of the participants indicated cutaneous reactions followed by gastrointestinal, respiratory, cardiovascular, nasal, ocular, and other signs. Moreover, the allergic participants were also inquired about drug dosage form to which the majority (18/23) identified oral dosage form followed by injectable i.e. intravenous and intramuscular. Very few participants (2/23) reported the usage of multiple dosage forms as shown in Figure 3.

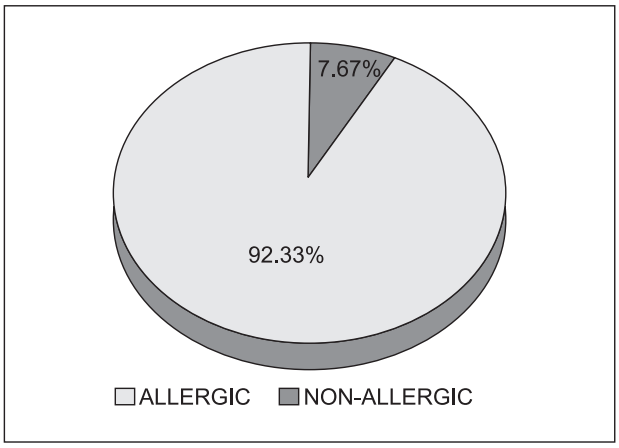

Fig 1: Frequency of self-reported drug(s) allergy

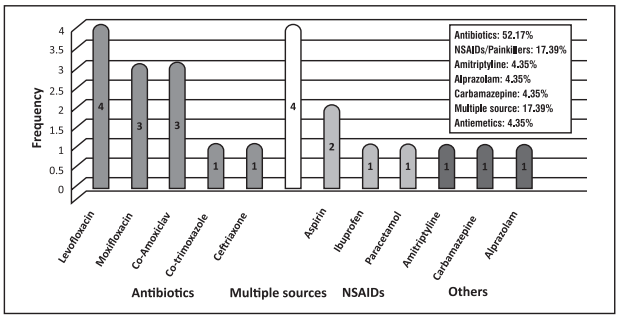

Fig 2: Distribution of sources of drug allergy

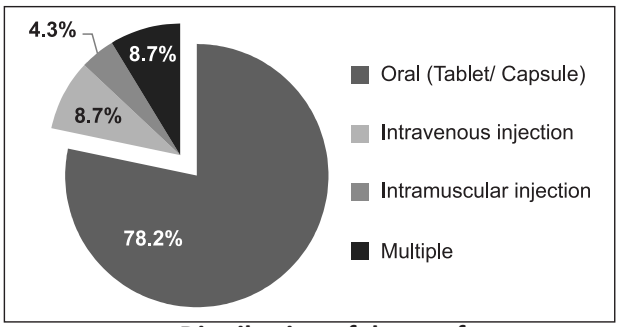

Fig 3: Distribution of dosage form

Table 1: Distribution of clinical manifestations of drug allergy

Clinical Manifestations	N (%)
Cutaneous Hives, Skin rashes, Urticaria, Pruritis, Angioedema	8 (34.8)
Gastrointestinal Nausea, Vomiting, Diarrhea, Abdominal pain	4 (17.4)
Respiratory Throat obstruction, Cough, Wheeze, Difficulty in breathing, speaking, or swallowing	3 (13.4)
Cardiovascular Palpitation, Tachycardia	1 (4.3)
Eye Itching, Redness & Secretion	1 (4.3)
Nasal Sneezing, Itching, Secretion, Congestion	1 (4.3)
Fever, Hypotension, Fainting	1 (4.3)
Other	4 (17.4)
Total	23 (100)

DISCUSSION

Worldwide studies indicate that allergic reactions to the drug(s) are responsible for significant morbidity and mortality. It is estimated that 3-7% of the population experience adverse drug reactions but data regarding drug hypersensitivity in the general population remains largely unknown. The current study was an attempt to determine the magnitude of drug allergic reactions in our community. We included medical students (due to their medical knowledge) of Peshawar as appropriate representative of the general adult population because reports are suggesting the prevalence of these reactions similar in university students and the general population.[14, 16]

Our study indicated the frequency of self-reported drug allergy as 7.67% resembling the results of studies done in an adult population of Portugal with the frequency of 7.8% [14] and the United Arab Emirates with the frequency of 7%.[12] However, there are reported frequencies of drug allergies much higher in the surveys conducted in Brazil (12.1%), Turkey (13.4%), and Maputo state of Africa (25%).[13, 15, 17] On the other side, a Turkish study on medical students reported a drug hypersensitivity prevalence of 4.7%, relatively less than the frequency revealed in our study.[15] Hence, a huge disparity has been observed in the results of studies done previously regarding the subject matter. This could be due to variation in the target population like the general population, hospitalized patients, and medical students. Other possible explanations for the observed discrepancies may include the differences in sample size, data collection technique, prescribing patterns, and self-medication habits. In this study, 78.2% males were found to be drug allergic as compared to 21% females. This is not in concordance with the study done in the Portuguese population where females were significantly more likely to claim a drug allergy than men.[14] There has no significant association been observed or reported between the incidence of drug allergic reactions and gender.

In our study, majority of the participants indicated antibiotics as their source of drug allergy followed by NSAIDs/painkillers resembling the results of many studies done globally.[11, 14, 17-20] However, there are reports where NSAIDs were identified as the most frequently associated drugs with allergic reactions.[13, 21, 22] The reason of this high frequency of antibiotic-induced allergy could be lack of regulation in the sale of antibiotics in our country, causing over-exposure of the general population to self-medication. Among antibiotics, surprisingly the highest frequency of allergy was observed with levofloxacin, unlike other studies where beta-lactams were reported as commonly involved antibiotics.[11, 13, 21] This discrepancy may be attributed to physician/patient preferences for levofloxacin over beta-lactams. Clinical manifestations of drug allergy were classified as cutaneous, ocular, respiratory, cardiovascular, and digestive signs. Our findings regarding cutaneous reaction as a common sign of allergy comply with many other studies done in the past.[11, 13, 23, 24]

In this study, the most important limitation lies in the precise differentiation of immune-mediated and non-immune mediated ADRs. A person giving a history of drug allergic reaction may not be allergic to it for several reasons i.e. reaction may have been due to a disease, a combination of drugs, presence of other factors like recall bias, etc. As our study population was medical students, some of them may have self-diagnosed themselves. Moreover, the generalizability of our findings to the whole community is not yet possible due to the small sample size and non-probability sampling technique adopted for this study. Despite these limitations, it was the very first attempt to provide epidemiological data regarding self-reported drug allergic reactions in the region.

CONCLUSION

Self-reported allergic reactions to the drugs were highly prevalent in the study population. Antibiotics were the most common source of drug allergies followed by NSAIDs with cutaneous manifestations as the most common sign of drug allergy. The high prevelance necessitate education of patients about the managment of drug allergies while prescribing drugs.

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AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under

Faisal MS:	Concept, study design and manuscript write up
Amin RU:	Data collection
Ahmad MS:	Data collection
Jamal A:	Data analysis and interpretation
Hayat W:	Statistical analysis, Bibliography
Haq KU:	Execution of study and critical review

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

ORIGINAL ARTICLE

MALNUTRITION IN CHRONIC KIDNEY DISEASE PATIENTS- A STUDY AT A TERTIARY CARE HOSPITAL

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ABSTRACT

Objective: To determine the frequency of malnutrition in patients with chronic kidney disease (CKD)

Materials and Methods: This cross-sectional descriptive study was conducted at the Department of Nephrology, Lady Reading Hospital, Peshawar from 15-06-2020 to 15-12-2020. CKD patients aged 20 to 80 years (mean age 53.55+ 8.078) were enrolled and assessed for malnutrition using Mini Nutritional Assessment (MNA) Score. Patients with MNA® of 0 to 7 were labeled as malnourished. Data were analyzed using SPSS version 23.

Results: A total of 170 CKD patients were enrolled. Among them, 118 patients were male and 58 females. The male to female ratio was 2:1. Malnutrition was observed in 65 patients (38.2%). Malnutrition was significantly associated with age of the patient ($p = 0.05$) and duration of CKD ($p = <0.001$).

Conclusion: Malnutrition was found in 38% of patients with CKD on hemodialysis. Patients with prolonged illness and advanced age are more likely to suffer from this condition.

Key Words: Chronic kidney disease (CKD), Malnutrition, Hemodialysis.

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INTRODUCTION

The Kidney Disease Quality Outcome Initiative has defined chronic kidney disease (CKD) as kidney damage or glomerular filtration rate (GFR) <60 mL/min/1.73 m2 for 3 months or more, irrespective of the cause. [1] It is one of the major public health concerns with an overall prevalence of 13.4% and the number of patients with kidney disease requiring replacement therapy is estimated between 4.9 to 7.0 million. [2]

Our country is no exception to this considerably high prevalence of CKD. Reports of a population-based cross-sectional study conducted in our country showed that the crude prevalence of chronic kidney disease is approximately 5.3% with diabetes and hypertension being the leading underlying etiology. [3] The clinical profile of CKD-related complications is very wide-ranging from cardiovascular complications to endocrine, gastrointestinal, and metabolic disorders. Malnutrition is one of the known complications of CKD. [4] Malnutrition is defined as an imbalance between nutrient requirement and intake resulting in cumulative deficits of energy, protein, or micronutrients that may negatively affect growth, development, and other relevant outcomes. [5] The approximate prevalence of malnutrition in CKD patients is about 31%. [6] The underlying mechanism for malnutrition in CKD patients is the cumulative effect of several derangements ranging from decreased oral intake due to uremia, the edematous small intestine lining creating hindrance to the absorption of nutrients, increased loss of nutrients e.g., proteinuria, hormonal and enzymatic disturbances leading to an imbalance in the metabolism of various macro and micronutrients. [7] A study by Ahmed K et al., reported a 42% prevalence of malnutrition in chronic kidney disease. [8] In a comparative descriptive study of nutritional assessment in CKD patients versus non-CKD patients, with blood hemoglobin level as a predictor of nutritional status, it was reported that low hemoglobin level was more prevalent in CKD patients compared to non-CKD. [9]

Malnutrition is a frequent finding in patients with chronic kidney disease on maintenance hemodialysis. The pathophysiology is complex and multifactorial. Suppression of digestive hormones stimulating the appetite is shown to play a key role in the development of malnutrition in patients with chronic kidney disease through loss or reduction of appetite. Similarly, reduction in sensitivity to insulin and subsequent dysregulation of glucose is also shown to be pivotal. [10] Other mechanisms include alteration in the normal gut flora in uremic patients, high circulating of inflammatory cytokines leading to hypoproteinemia due to chronic inflammatory state. Chronic in-

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flammation further suppresses appetite. Cumulative effect poses the patient to malnutrition. [11]

Comprehensive studies on the assessment of nutritional status in chronic kidney disease in our local population are lacking. So, this study is aimed to assess the nutritional status of chronic kidney disease patients presenting to the Nephrology Unit of Lady Reading Hospital, Peshawar. the results of the study will emphasize the importance of correcting the nutritional status of patients with CKD.

MATERIAL AND METHODS

This Cross-sectional was conducted at the Department of Nephrology, Lady Reading Hospital Peshawar with the permission of the ethical review committee of the hospital from 15-06-2020 to 15-12-2020. Patients were recruited through a convenient sampling method. Both male and female patients with chronic kidney disease with the age range of 20 to 80 years were included. Both pre-dialysis and patients undergoing dialysis were included.

Chronic kidney disease was confirmed based on KDIGO criteria that included 1) routine examination of urine sample positive for markers of kidney damage e.g. albuminuria. 2) eGFR less than 60mL/min/1.73m2), imaging studies supporting chronic kidney disease e.g. ultrasound study showing cortical thickness less 6 mm, renal length less than 8 cm, irregular margins, and increased renal cortical echogenicity. The persistent presence of any two for more than 3 months was considered confirmatory for chronic kidney disease. Patients with a history of hypothyroidism, malabsorption disorders, chronic liver disease, malignancy, and chronic infective conditions like tuberculosis were excluded.

Patients with chronic kidney disease were enrolled from the indoor department of Nephrology, Lady Reading Hospital, Peshawar. Demographics including age, gender, height, weight, and BMI were noted. Information regarding etiology, duration of CKD, and dialysis (pre-dialysis/post-dialysis) were recorded. Nutritional status was assessed using MNA proforma consisting of six components including appetite change, unintentional weight loss, mobility, psychological issue, neuropsychological disorder, and BMI. Score 0 to 7 was labeled as malnourished. Blood metabolic profile was determined in the blood samples of patients in the hospital laboratory for serum calcium and serum albumin. Serum calcium less than 8.6 mg/dl and serum albumin less than 3.5 gm/dl were considered positive for malnutrition. Data were analyzed using SPSS version 23. Means (with standard deviations) were calculated for quantitative variables including age, duration of CKD, height, weight, BMI, serum calcium, and serum albumin. Qualitative variables including gender, etiology of CKD, dialysis status, and malnutrition were presented in frequencies and percentages. Statistical tests of significance included the student t-test for continuous variables and the chi-square test was used for categorical variables. Chi-square of independence with Cramer V nominal was applied for the association of malnutrition with age groups, gender, BMI status, dialysis status, and etiology of CKD. p-value ≤ 0.05 was considered statistically significant.

RESULTS

A total of 170 patients fulfilling the inclusion criteria were studied. The age of the patients ranged from 20 to 80 years. The mean age was 53.55(±8.078 SD) years. One-hundred and fifty-three patients (90%) belonged to the age group 41-60 years. Out of 170 patients, 118 patients (69.4%) were males and 52 patients (30.6%) were females. The male to female ratio was approximately 2:1. The mean BMI of the patients was 24.8 (±2.67 SD) Kg/m^2. The majority of the participants (102 patients) had BMI in the range of 19.1- 25.0 Kg/m^2. Diabetes mellitus was the most common underlying etiology of CKD. It was observed in 114 patients (67.1%) followed by hypertension (see table-1). CKD duration was grouped into patients having CKD duration less than one year and patients having CKD duration of more than one year. 110 patients (64.7%) had a CKD duration of more than 1 year.

According to MNA Score, malnutrition was observed in 65 patients (38.2%). Mean serum calcium and mean serum albumin in patients with positive malnutrition were 8.17 (±1.951SD) mg/dl and 3.2 (±0.99 SD) gm/dl.

DISCUSSION

In our study, malnutrition was observed in 38.2% of patients with chronic kidney disease. Results of the study conducted by Ahmed KA and colleagues are higher as compared to the results of our study who reported malnutrition in 63.3% of patients with chronic kidney disease. [8] This disparity could be attributed to more number of male participants in our study. In general, nutritional status in our country isn't satisfactory but females are more prone to undernutrition compared to men. [12] Though this study could not establish a significant association between gender and malnutrition (p-value = 0.468), the proportion of females with malnutrition was higher compared to male patients (42.3% vs. 36.4%). The mean age of the patients was 53.55 (±8.078SD) years. Results of our study are comparable to the reports of a Moroccan study where the reported mean age was 52±12 years. [13] However, a much higher mean age has been reported in such patients in a study conducted in the western population. [14] A significant association was observed between malnutrition and age (p-value = 0.05). A rising trend was observed in the proportion of malnutrition with advancing age. This effect could be explained by the cumulative effect of degenerative changes with rising age and dysmetabolism in uremic patients.

Table 1: Patient baseline characteristics and association with malnutrition

		Malnutrition		p-Value
		Yes	No	
Age	20-40	3(100.0%)	0(0.0%)	0.050
	41-60	55(35.9%)	98(64.1%)	
	61-80	7(50.0%)	7(50.0%)	
Gender	Male	43(36.4%)	75(63.6%)	0.468
	Female	22(42.3%)	30(57.7%)	
BMI (kg/m2)	19.1-25.0	39(38.2%)		0.388
	25.1-30.0	25(41.0%)	36(59.0%)	
	30.1-35.0	1(14.3%)	6(85.7%)	
Etiology of CKD	DM	38(33.3%)	76(66.7%)	0.285
	Hypertension	12(46.2%)	14(53.8%)	
	Glomerulonephritis	4(66.7%)	2(33.3%)	
	Interstitial Nephritis	2(33.3%)	4(66.7%)	
	Misc. Causes	9(50.0%)	9(50.0%)	
Dialysis Status	Pre-Dialysis	35 (37.6%)	58(62.4%)	0.859
	Post Dialysis	30(39.0%)	47(61.0%)	
CKD Duration	Less than 1 year	7(11.7%)	53(88.3%)	<0.001
	More than 1 year	58(52.7%)	52(47.3%)	

A significant association was observed between the duration of chronic kidney disease and malnutrition in our study. The effect could be explained by the prolonged exposure of CKD patients to continuous oxidative and inflammatory stress combined with dysregulation of gut bio-flora and hormonal imbalance. [15] On the other hand, Adejumo et al., failed to report a significant effect of prolonged illness on malnutrition in the absence of function of kidneys.[7] Diabetes mellitus was the most common cause of chronic kidney disease in the study participants (67% patients), followed by hypertension (15.3% patients). This study could not establish a significant effect of the etiology of CKD on malnutrition. Similarly, no significant association was observed between BMI and malnutrition. This result disagrees with the report of the study conducted by Srinivasan et al., who reported a significant association between malnutrition and BMI with malnutrition being more prevalent in underweight patients. [14] It may be due to the effect of extracellular and third space fluid collection on the weight of study participants. To control this bias, the lower limit of healthy BMI range was raised to 19 kg/m2 in this study compared to the routine 18.5 kg/m^2. Had this bias been controlled by dry and wet weight, the results might have been different.

This study has some limitations. Of most importance is a single-center study with a limited number of patients to find the true relationship of the prevalence of malnutrition in CKD and its association with other variables like duration of disease, cause of CKD, and other factors. Large-scale multicenter studies are needed to address these and other issues.

CONCLUSION

Malnutrition was found in 38% of patients with CKD on hemodialysis. Patients with prolonged illness and advanced age are more likely to suffer from this condition.

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AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under

Muhammad S: Idea and writing of the manuscript.

Ikram M: Data collection

Roghani Z: Data and Statistical Analysis

Khursheed M: Overall supervision of the study during collection of data and compiling, corrections and re writing

Ghulam S: Collection of data and compiling, corrections and re writing

Hanif M: Bibliography

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

ORIGINAL ARTICLE

THE EFFECTIVENESS OF DIFFERENT INSULIN REGIMENS IN DIABETIC PREGNANT PATIENTS- A RANDOMIZED CONTROLLED TRIAL

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ABSTRACT

Objective: To compare the effectiveness of Basal bolus and Premixed Insulin regimen in gestational and type 2 diabetic pregnant patients.

Material and methods: This randomized controlled trial was conducted in Obstetrics and Gynecology department, Lady Reading Hospital (LRH) Peshawar over a period of one year from January to December 2020. A total of 100 patients with Type 2 Diabetes and Gestational Diabetes were included in the study. These 100 patients were divided into two groups. Group 1 was allocated to patients given Basal Bolus Regimen and Group 2 was allocated to patients given Pre-mixed twice daily Insulin. Patients were allocated to each group randomly by lottery method. The patients were put on insulin according to body weight after the first 24-hour blood sugar profile.

Results: The two groups were comparable for maternal age (34.6±4.68, 34.6±5.11, p-value = 0 .775), gestational age (34.2±1.65, 34.0±1.34, and p value = .552), gravidity (7.08±1.65, 6.68±1.5, p-value of 0.434). HBA1C in the two groups were similar (7.40±.742 and 7.39±.751 with a p-value of 0.947), with mean blood glucose (calculated by average of 2 readings of postprandial levels) in the two groups in first 24 hours were comparable (MBG 24Hrs Group 1= 341.54±46, Group 2 =344.08±47 p-value = 0.784). There was a rapid control of blood sugar, on day 7 with Basal Bolus regimen with Mean Blood Glucose (MBG) 152±9.798mg/dL as compared to Premixed split regimen which was 192.4±14.99 mg/dL

Conclusion: The Basal bolus regimen is more effective than the premixed insulin regimen in controlling blood sugar in pregnant patients with diabetes.

Key words: Multiple dose Insulin (MDI), Mean blood glucose (MBG), Gestational Diabetes Mellitus (GDM)

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INTRODUCTION

Diabetes is the most common disorder affecting about 7% of pregnancies where 87.5% of these females have gestational diabetes, 7.5% have type 1 diabetes while 5% have type 2 diabetes.[1,2] Gestational diabetes mellitus is defined as a fasting blood sugar(FBS) of 100 mg/dl or more and 2 hours' random blood sugar (RBS), postprandial of 140 or more on 75 gm OGTT after 24 weeks of gestation. Type II Diabetes is characterized by FBS more than 126mg/dl before 24 weeks of gestation of pregnancy[2].

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The poor metabolic control in diabetic patients leads to unfavorable fetal outcome. The choice of treatment in pregnancy is insulin. Two types of conventional insulin regimens i.e. the Premixed regimen and the basal bolus regimen are used which mimic endogenous insulin response. Premixed or split regimen is defined as premixed 70/30 formulation having 30% Regular insulin and 70% NPH given BD before meals with 2/3rd of total calculated dose given in the morning and 1/3rd of the dose given in evening. The advent of Insulin analogues with improved pharmacokinetics has resulted in pregnancies with good maternal and fetal outcomes[2,3]. Trials have also shown safety of oral hypoglycemic especially metformin and glyburide to warrant use in pregnancy[4]. Whatsoever be the type or regimen of insulin used the main aim is to achieve a good glycemic control so as to reduce maternal and fetal complications. The best insulin regimen would be the one which controls the mean blood glucose (MBG).

The aim of our study was to compare the conventional regimens so as to device a protocol of which one

is better in pregnancy for use in our patient as both the regimens are in affordable ranges as compared to Insulin analogues.

MATERIAL AND METHODS

This study was done in Obstetrics and Gynecology department of Lady Reading Hospital from January 2020 to December 2020. It was a Randomized controlled open labeled study. The sample size was 100 calculated with WHO formula taking the prevalence of diabetes in pregnancy as 7%, confidence interval 95% and margin of error 5%. The patients were distributed in the two groups randomly by lottery methods. The inclusion criteria were pregnant patients with GDM and type II diabetes, booked in first, second and third trimester before 32 weeks of gestation. The exclusion criteria were patients booked in late 3rd trimester after 32 weeks, Type 1 diabetics, patients already controlled on oral hypoglycemic agents. Data was entered to SPSS 24, mean ±SD was calculated for continuous variable like age, period of gestation, parity and mean blood glucose. Post stratification analysis was done using independent "t" test to calculate p value ≤ 0.05. In this study 50 patients were put on basal bolus regimen in Group 1 and another fifty patients were given premixed regimen in Group 2, after consent from each patient. Patients were booked through antenatal clinic, admitted for work up which included 6 points blood sugar profile and HBA1C. After 24 hours' blood sugar levels patients were put on one of the regimens according to body weight in kilograms with this formula.

Body weight in Kg x 0.6 in first trimester = Total units of insulin to be started for the patient. Body weight in Kg x 0.7 in second trimester = Total units of insulin to be started for the patient.

Body weight in Kg x 0.8 in second trimester = Total units of insulin to be started for the patient. Total units of insulin in premixed regimen were given twice a day in the formulation of 70/30 (two third of NPH in this formulation and with one third of Regular insulin).

Total units of insulin in Basal Bolus Regimen were given according to the following formula with one fourth of NPH given at night at 10 pm and rest of Insulin was given as Regular Insulin and this Regular Insulin was divided into equal dosages as thrice a day (6 hours' interval) and half an hour before meals.

The efficacy parameters were time and doses needed to control the blood sugar. Patients were given dietary counseling sessions with easy pictorial diet charts and were advised to walk for 30 minutes every day. All this information was filled on a proforma, the patients were followed up in the OPD after every 2 weeks with their blood sugar records and fetal surveillance. If the blood sugars were abnormal then the patients were readmitted.

RESULTS

The two groups were similar for maternal age, gestational age, gravidity, mean blood glucose in first 24 hours as shown in Table 1.The first 24 hour MBG was 341.54±46mg/dL and 344.08±47 mg/dL in basal bolus and premixed regimen group respectively with a p-value of 0.784 as given in Table 1. MBG was calculated by average of 2 readings of postprandial levels. The MBG on day 3 being 160.20±8.569 mg/dL in basal bolus group and 222.22±17.57 mg/dL in premixed insulin. There was a rapid control of blood sugar, on day 7 in basal bolus group with 152±9.897 mg/ml as compared to premixed regimen which was 192.42±14.99 mg/dL with a p-value of 0.000 as shown in Table 2.

DISCUSSION

The ultimate goal of using different insulin regimens in pregnant diabetic patients is to attain a near normal glycemic control to avoid fetal complications like fetal congenital anomalies, polyhydramnios, fetal macrosomia which in turn leads to intrapartum and post-partum complications.

Table 1: Demographic data of Pregnant Diabetic patients

Variables	Basal bolus regimen	Premixed Regimen	P value
Maternal age	34.6±4.68	34.6±5.11	.775
Gestational age	34.2±1.65	34.0±1.34	.552
Gravidity	7.08±1.65	6.68±1.56	.434
Hba1c	7.40±.742	7.39±.751	.947

Table 2: Control of mean blood glucose by Basal bolus and premixed regimens

	Group 1 Basal Bolus Regimen	Group 2 Premixed Insulin 70/30
No of patients in each group	50	50
Type 2 Diabetics	38	39
Gestational Diabetics	12	11

Table 3: Time required controlling the blood sugar with basal bolus regimen versus premixed regimen

Variable	Basal bolus regimen	Premixed regimen	P value
MBG 24Hrs	341.54±46	344.08±47	.784
MBG 72Hrs	160.20±8.569	220.22±17.57	.000
MBG 7days	152.00±9.897	192.42 ±14.99	.000

Table 4: Side effects associated with Insulin Regimen

Variable	Basal Bolus Regimen	Premixed regimen	P value
Hypoglycemia	0	5	NC

Current study shows that study basal bolus regimen is more effective in controlling blood sugar levels in gestational as well as type 2 diabetic pregnant patients as compared to pre-mixed regimen in lowering mean blood glucose levels more efficiently. Similar observation was noted in studies done by Nachum S Z and Kernaghan D[5,6]. A basal-bolus routine involves taking a longer acting form of insulin to keep blood glucose levels stable through periods of fasting and separate injections of shorter acting insulin to prevent rises in blood glucose levels resulting from meals. One of the main advantages of a basal-bolus regimen is that it allows to closely match how body releases insulin in a natural way if it was able to do so.

Patients in both the groups upon admission had uncontrolled diabetes as can be seen from their mean 24-hour admission blood glucose levels and HbA1C (as shown in Table. 1), but then had a sustained control of blood sugars in the following weeks of pregnancy with basal bolus regimen.

Although lowering of blood glucose was noticed in the premixed insulin regimen also, but a more rapid control was achieved with basal bolus as compared with premixed insulin (mean blood glucose MBG of 152±9.897 mg/dL vs. 192.42±14.99mg/dL) respectively as shown in Table 2.

This study was performed in low economic resource setting with non-availability of medicines. In our study both types of insulins were less expensive, with the basal bolus regimen giving a good control of blood sugars same as with ultra-short acting insulin[7].

Another study done by Jovanovic supported the use of Basal bolus regimen with good fasting and HBA1c control[8]. Although the four-dose daily regimen involves more injections a day than a twice daily regimen, the twice daily regimen entails frequent changes in the dose adjustment. Additionally, patients with basal bolus regimen may have meals at more flexible intervals as they can adjust the dose of insulin to variables such as exercise and appetite[9,10].

A study done by Ranasingh PD et al. recommends the use of Insulin according to individual cases with the use of multiple dose regimen being the most common[11]. A review of 5 randomized controlled trials revealed no firm conclusions that which Insulin type is better[12]. A review of recent advances and current trends by Nawaz et al showed that multiple insulin injections were one of the best treatments to control diabetes[13]. In our study patients were admitted twice or thrice for control of blood sugars during the antenatal period because of their noncompliance and inability to check blood sugar on glucometer or laboratory. Multiple admissions to hospital lead to better blood sugar control[14]. In our study as shown in Table 4 the incidences of hypoglycemia were low in both groups.[15] With the evidence from our study and comparisons with the other studies we can clearly see that the basal bolus regimen is effective, as compared with premixed regimen. We have not compared other types of Insulin in pregnant diabetic patients. Further large-scale studies are required to compare different Insulin regimen in pregnant diabetic patients. Different types of Insulin are to be compared for a better control of blood glucose levels in our pregnant population.

CONCLUSION

The results of our study revealed that Basal bolus regimen is more effective than the premixed insulin regimen in controlling blood sugar in pregnant patients with diabetes.

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AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under

Sabir SA: Concept/ Idea, Literature, review, Drafting & Final Review

Qazi Q: Manuscript Writing, Literature review, Analysis & Interpretation of Data

Abbas G: Concept/idea, Data Collection

Zeb L: Concept/idea, Literature review, Drafting & Final Review

Yasmin S: Concept/idea, Literature review

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

ORIGINAL ARTICLE

THE FREQUENCY, TYPES AND RISK FACTORS OF URINARY INCONTINENCE IN WOMEN PRESENTING TO THE GYNAECOLOGY OUTPATIENTS OF A TERTIARY CARE HOSPITAL

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ABSTRACT

Objectives: To determine the frequency, types, and risk factors of urinary incontinence in women presenting to the Gynaecology outpatient department of a tertiary care hospital

Materials and Methods: This was a cross-sectional study conducted at the consultants' clinics of Lady Reading Hospital, Peshawar, from October 2019 to September 2020. Five hundred and sixty women aged more than 18 years were interviewed through a questionnaire. The questionnaire contained information regarding Age, Parity, BMI, and types of Urinary Incontinence. Data were analyzed using SPSS-23 where frequencies and percentages were used for categorical variables and mean and SD for numerical variables.

Results: The overall frequency of urinary incontinence was 32.5% (n=182) and showed an increasing trend with age, BMI and parity. The mean age of the sample was 56.16 years (±9.67), mean BMI of 30.10 kg/m2(±4.29),and mean parity of 4.49 (±1.39). The final logistic regression model showed that increasing age [OR: 0.9 95% CI: 0.6–1.49], BMI more than 30 kg/m2 (OR 0.63, 95% CI: 0.43–0.94), and mean of six children delivered (OR 0.95 95% CI: 0.59–1.53) were associated with increased odds of having urinary incontinence. The distribution of urge urinary incontinence, stress urinary incontinence and mixed urinary incontinence was 40.11% (n=73), 35.71% (n=65), 24.73% (n=45) respectively.

Conclusion: Almost one-third of the women attending consultant gynecological clinics had some form of urinary incontinence. The severity of urinary incontinence was associated with age, BMI, and parity.

Key words: urinary incontinence, Age, Parity, BMI

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INTRODUCTION

Urinary incontinence is a common problem affecting women in the middle age as well as in the peri and postmenopausal age group [1,2]. The International Continence Society (ICS) has defined urinary incontinence as "the complaint of any involuntary leakage of urine" [3,4]. Severe urinary incontinence might have a significant effect on women's lives[5,6], but even mild urinary incontinence can distinctively affect daily life. Based on symptoms, urinary incontinence is mainly divided into stress incontinence, urge incontinence, and mixed symptoms.

Prevalence estimates for urinary incontinence are extremely varied even in the international literature. This variation has been attributed to the different definitions of urinary incontinence, different characteristics of the studied population, and different data collection methods e.g. postal questionnaire, reporting personal interviews, or clinical assessment[7,8]. Prevalence rates are varied between 12% and 53% in a review of 48 epidemiology studies[9]. A study in 2016 showed a median prevalence of 27.6% in urinary incontinence among females of different non-institutional populations[10]. There is a lack of significant studies on the Pakistan population which gives an epidemiological outlook to this problem. It is however of value to determine the spectrum of urinary incontinence in our population.

Certain factors influence the development of urinary incontinence in females. It has been found that age, education, reproductive history, BMI, chronic medical diseases, personal and social factors have a direct or indirect effect on urinary incontinence[11].

The lack of any robust data on the prevalence of urinary incontinence in our population led us to conduct this cross-sectional study. The main objective of this study was to determinethe frequency, types, and risk factors of

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urinary incontinence in women presenting to the Gynaecology outpatient department of Lady Reading Hospital Peshawar.

MATERIAL AND METHODS

This cross-sectional study was conducted among women attending consultants` clinics in the Outpatient Department of Gynaecology, Lady Reading Hospital, Peshawar. The study was conducted from October 2019 to September 2020. The protocol was approved by the Ethical Board Medical Teaching Institution, Lady Reading Hospital, Peshawar.

The participants were enrolled in the outpatient department Lady Reading Hospital, Peshawar. The study report included all women aged >18 years. Urinary incontinence was defined as leakage of urine at least once during the past four weeks as described by the International Continence Society (ICS). [12]

Data was collected using a questionnaire by the consultants and nurses working with the consultants in OPD and clinics. During the personal interview, the study was explained and informed consent was taken. Pregnant women were excluded from the study. Data were analyzed using SPSS-23 where frequencies and percentages were used for categorical variables and mean and SD for numerical variables.

RESULTS

A total number of 560 consecutive women were eligible for recruitment, October 2019 to September 2020. One-hundred and eighty-two women gave a history that they had experienced urinary incontinence in the last four weeks, giving an overall prevalence of 32.5%.

The mean age of patients was 56.16 years (±9.67), had a mean BMI of 30.10 kg/m^2(±4.29), and delivered a mean number of 4.49(±1.39) children. The incontinent women were older (56.16 years vs 36 years), had a higher BMI (30.10 kg/m^2 vs 26.8 kg/m^2), and delivered more children (4.49 vs 4.0) than continent women. Independent two-sample T-test was used to calculate P-values (Table-I)

The overall frequency of urinary incontinence in the study group was 32.5%. It showed an increasing trend with an increase in age, BMI, and parity. In the final logistic regression model, age 60–69 years. [OR: 0.9 95% CI: 0.6–1.49], BMI more than 30 kg/m^2 (OR 0.63, 95% CI: 0.43–0.94) and mean of six children delivered (OR 0.95 95% CI: 0.59–1.53) were associated with increased odds of having urinary incontinence. (Table No.3)

The type of urinary incontinence was evaluated in women presenting with incontinence of urine. The distribution of urge urinary incontinence, stress urinary incontinence and mixed urinary incontinence was 40.11% (n=70), 35.71% (n=65) and 24.73% (n=45), respectively. Urge urinary incontinence and stress urinary incontinence was predominant in women aged 55 years (±9.30), whereas mixed urinary incontinence was more prevalent in older women (P= .04). Women with urge incontinence had higher BMI.

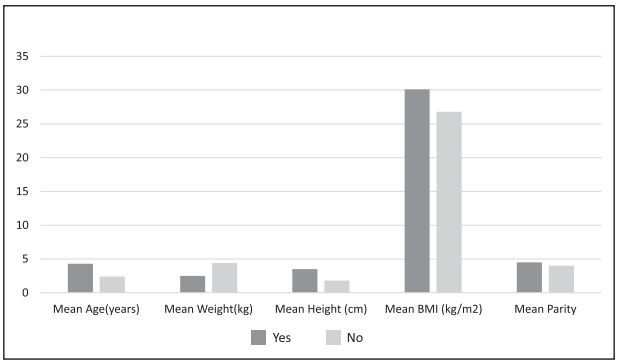

Fig 1: Demographic characteristics of participants

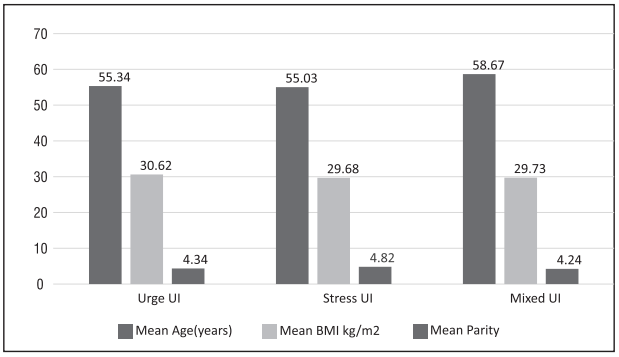

Fig 2: Urinary incontinence and clinical and demographic characteristics

Table 1: Demographic characteristics of the participants (Total=560)

	Variables	Urinary Incontinence		P. Value
		Yes (n = 182)	No (n = 378)	
1	Mean Age (Year)	56.16 (±9.67)	36	0.00
2	Mean Weight (kg)	71	67	
3	Mean Height (cm)	157.48	158.60	
4	Mean BMI (kg/m2)	30.10 (±4.29)	26.8 (±4)	0.00
5	Mean Parity	4.49 (±1.39)	4 (±1)	0.00

Table 2: Frequency of urinary incontinence to clinical characteristics

Age (Years)	Numbers (560)	Percentage	Odds Ratio (95%CI)
18–29	23	4.34 (1)	1
30–39	67	16.41 (11)	0.23 (0.03–1.9)
40–49	112	20.53 (23)	0.76 (0.34–1.68)
50–59	162	40.74 (66)	0.38 (0.22–0.66)
60–69	173	41.61 (72)	0.96 (0.62–1.49)
70+	23	39.13 (9)	1.11 (0.46–2.7)
BMI (kg/m2)			
< 25	119	16.8 (20)	1
25–30	238	31.93 (76)	0.43 (0.25–0.75)
≥ 30	203	42.36 (86)	0.63 (0.43–0.94)
Parity			
1	20	10% (2)	1
2–3	173	23% (40)	0.37 (0.08–1.66)
4–5	267	38% (101)	0.49(0.32–0.76)
6+	100	39% (39)	0.45 (0.59–1.53)

Table 3: Urinary incontinence and clinical and demographic characteristics

	Urge UI	Stress UI	Mixed UI
Mean Age (Years)	55.34 (19.30)	55.03 (±10.57)	58.67 (±8.97)
Mean BMI (kg/m2)	30.62 (±3.60)	29.68 (±4.76)	29.73 (±4.66)
Mean Parity	4.34 (±1.26)	4.82 (l 1.61)	4.24 (±1.15)

DISCUSSION

This cross-sectional study assessed the frequency of urinary incontinence in women > 18 years and the clinical characteristics of women presenting with different types of UI. Overall 32.5% experienced UI at least once per month. The frequency of urinary incontinence increased with age, BMI and parity. Urge incontinence was the commonest type of urinary incontinence, followed by stress urinary incontinence and mixed urinary incontinence.

There have been very few studies assessing prevalence rates of female urinary incontinence in local literature. Most of the local literature shows a wide prevalence range of 11.5% and 44.4% [13,14,15]. Our findings are consistent with the above mention studies. In Pakistan, life expectancy is lower as compared to other regions of the world, as a result lesser number of elderly women were part of the cohort. However, early age of menopause and less frequent use of hormone replacement therapy makes our population more vulnerable to lower urinary tract dysfunction.

Even international literature assessing prevalence rates of urinary incontinence gives a range between 24.5% and 49.7%[16-20]. A Turkish study using a validated questionnaire indicated a 25.8% prevalence rate in women over 20 years of age[18], which was similar to a French study [(1)] showing a prevalence rate of 26.8%. The prevalence rate of 26.3% was reported in the community developing Australian women over 20 years of age[19]. Abramas et al. reported 25% overall and 7% severe urinary incontinence at a similar age group in Norwegian women[20]. The overall prevalence rates (32.5%) were higher than the above studies but lower than France (44%), Germany (41%), and UK (42%)[20].

In the present study, the rate of urinary incontinence increased with age, BMI, and increasing parity. Indeed age > 50years, BMI > 25kg/m^{2,} and delivery of more than 3 children were the most predictive factors. These risk factors confirm those described in the literature [21,22].

In our sample, urge incontinence was the predominant form of urinary incontinence, followed by stress urinary incontinence and mixed urinary incontinence. The highest rate of urge urinary incontinence was found in women aged 70 years and more.

Stress urinary incontinence was predominant before the age of 70 years, while mixed urinary incontinence was more common in the age range of 60–69 years. The highest rate of stress incontinence was in women between 30–39 years of age. These findings are in agreement with French[1] and a Turkish Study[3]. Local literature however shows stress urinary incontinence as most commonly reported subtypes.

Similar to age, BMI and parity were significant variables in the prevalence of urinary incontinence. Parity was the main risk factor for stress urinary incontinence whereas BMI was a significant variable in urge urinary incontinence[15].This validates the findings in a study done at Agha Khan University Hospital, Karachi. They have also evaluated the effect of mode of delivery on prevalence of stress urinary incontinence. They found it is the pregnancy rather than mode of delivery which contributes to the development of stress urinary incontinence. Our study demonstrated that urinary incontinence is widespread in women attending gynecological clinics.

A few limitations of the present study should be considered. First, this study was dependent on patients' history and no tool was used to confirm it objectively. Moreover, it is a single-center study involving mostly the Pathan population. Further multicenter studies with more objective evidence of UI are required to strengthen the prevalence of this condition at the national level.

CONCLUSION

Almost one-third of the women attending consultant gynecological clinics had some form of urinary incontinence. The severity of urinary incontinence was associated with age, BMI, and parity.

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AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under

Fahim F: Concept/ Idea, Literature, review, Drafting & Final Review

Fahim WB: Manuscript Writing, Literature review, Analysis & Interpretation of Data

Zahoor F: Concept/idea, Literature review, Drafting & Final Review

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

ORIGINAL ARTICLE

EFFECTIVENESS OF DRY NEEDLING ON THE LUMBAR PARASPINAL MUSCLE IN PATIENTS WITH MECHANICAL BACK PAIN: A RANDOMIZED CONTROLLED TRIAL

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ABSTRACT

Objective: The aim of this study was to compare the effect of dry needling and sustained pressure in the lumbar paraspinal trigger points in terms of pain threshold and muscle length.

Material & Methods: Fifty patients were randomly allocated in experimental and control group having lumbar paraspinal muscle trigger points. Experimental and control groups received dry needling and sustained pressure along with stretching and strengthening exercises. Patients were assessed at 1st pre-and 4th post session using Oswestry disability index, paraspinal muscle length, visual analogue scale and pain pressure threshold using algometer.

Results: Pain pressure threshold and visual analogue scale showed significant results whereas Oswestry disability index and paraspinal muscle length showed no significant results ($P>0.01$). Analysis within the group showed significant difference from pre-to post intervention level ($P<0.01$) in terms of pain pressure threshold, paraspinal muscle length, Oswestry disability index and visual analogue scale in experimental and control group.

Conclusion: Pain was improved using dry needling. However, no significant improvement was seen in patient's disability and lumbar paraspinal muscle length.

Key words: Dry needling, Oswestry disability index, Paraspinal muscle, Trigger points, Visual analogue scale.

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INTRODUCTION

Myofascial pain is a type of pain that emerges from muscles and related fascia which is typically related to myosfascial trigger points (MTrP). [1] MTrPs are hyperirritable spots in taut bands of skeletal muscles. Compression of the involved area elicits pain that may be radiating or localized in nature, produces local twitch response, painful on stretching along with other associated symptoms. [2] MTrPs can be categorized into active and latent, which are clinically different from one another. Active trigger points have referred pain and reproduces symptoms familiar to patient pain pattern evident in different musculoskeletal issues. On other hand, latent myofascial trigger points are tender points produces local twitch response, local or referred pain on manual examination and is not familiar or known by the patient. [3]

MTrP is considered as primary cause of most musculoskeletal pathologies. A research study conducted in united states reported that 30 to 85% of patients has MTrP as primary source of pain (1). Low back pain has a lifetime prevalence of 60%-80% among adult people and the most prevalent of all musculoskeletal concern in the western countries. [4,5] Erector spinae is the most common muscle prone to muscle spasm and cause low back pain. Trigger point present at erector spinae muscle results in radiating pain to buttock all the way from hip bone to the bottom crease. Muscles next to the spine are known as paraspinal muscles. A study conducted in Malaysia by Chen and nizar concluded that 63.5% patients having chronic low back exhibiting MTrP in lumbar paraspinal muscles and piriformis as a common source of pain. [6] One of the minimally invasive procedures used to treat MTrP is dry needling. In this procedure acupuncture needles are insert-

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ed at the site of taut bands or trigger points at the basic course of anatomy. [1]

There is no study present till now in which comparison of dry needling and sustained pressure was compared at lumbar paraspinal muscles. A study conducted on sustained pressure and dry needling at cervical region recommended additional research on sustained pressure and dry needling with high quality study design and more conclusive evidence. [7] The objective of this study is to compare the effect of dry needling and sustained pressure in the lumbar paraspinal trigger points in terms of pain threshold and muscle length.

MATERIAL AND METHODS

A randomized control trial was conducted at Riphah international hospital Islamabad and Pakistan railway general hospital Rawalpindi. The trial registration no is NCT04043741. The current study was approved by Riphah International University Ethical Committee (Riphah/RCRS/REC/00490).

Fifty patients diagnosed with lumbar paraspinal trigger points were randomly allocated into control (n=25) and experimental group (n=25). Informed consent was taken from each participant prior to participation. The study inclusion criteria were age from 20-50, patient having acute, sub-acute, chronic low back pain, Mechanical low back pain and radiculopathies caused by foramen encroachment and traumatic disc herniation up to one year and those patients having active spontaneously painful or latent requiring palpation to reproduce the characteristic pain MTrPs. However, Patients that were using any medication to reduce the pain and/or have any side effect on the skeletal muscle including analgesics, anticoagulants, and muscular relaxants, taking other treatment in the same period of the research, pregnant female, patients with Chronic Disease (kidney disease, Diabetic, and osteoporosis) and spinal diseases (herniated disc, spondylolisthesis) were excluded.

Patients were assessed on 1st pre-and 4th post session by using Visual analogue scale (VAS), Oswestry Disability Index (ODI) and Algometer to determine pain, disability and pain pressure threshold respectively.[5,8,10] Paraspinal muscle length (PML) was measured with the measuring tape. In paraspinal muscles length assessment, patients adopted sitting position.

The anterior superior iliac spine (ASIS) was palpated bilaterally and the patient was instructed to flex forward to produce pelvic tilt. When ASIS started to move, this was considered the end of thoracolumbar flexion and initiation of anterior pelvic tilt. According to Janda, patient forehead needs to come 10 inches of the knees normally. [11]

Screening for lumbar paraspinal myofascial trigger points was performed using manual palpation to assess whether myofascial trigger points were a contributing factor to the patient's reported low back pain. According to Travel and Simons, L1 trigger point is present at Iliocostalis muscle at upper lumbar level where pain is referred downward concentrating at mid-buttock, whereas, L2 trigger point is present at Multifidus muscle. On palpation, pain radiates anteriorly to the abdomen, that can be easily misjudged as of visceral origin. [12]

Prior to the procedure, signing the informed consent forms was done to satisfy the ethical requirements. After Ruling out any absolute contraindication, 4 sessions of trigger point dry needling at lumbar paraspinal muscles was done in experimental group on alternate days with exercise plan including stretching and strengthening exercises (3 sets into 15 reps). Same exercise plan was guided for home plan.

For lumbar paraspinal muscles dry needling, patient was asked to lie in a prone position. Skin was thoroughly cleaned using a cotton swab. The examiner palpated the muscle to recognize the taut band, and hyperirritable spot. Stainless steel filiform needle was used to perform the procedure of dry needling. By using flat palpation method, needling tube was fixed on targeted point at 45 degree; and needle was gently loosened from the tube. The apex of the needle was tapped allowing the needle to penetrate the skin deeply. [13] Once the needle had penetrated into the muscle, it was manipulated. Entire procedure took approximately 15- 20 minutes.

In control group, preceding the treatment, hot pack was applied at low back (15 mins). Four sessions of sustained pressure at lumbar paraspinal muscles were done on alternate days with exercise plan including stretching and strengthening exercises (3x15sets). Same exercise plan was guided for home plan. Sustained pressure is a manual release technique in trigger point therapy. During the procedure, clinician lengthened the muscle up to the increasing resistance within the comfort zone, and then gradually applied gentle pressure on Trp until fingers felt a definite increased in tissue resistance (first barrier). Patient felt only discomfort but no pain. Pressure was maintained at this point until clinician sensed relief of tension under palpating finger. This maneuver was continued until new barrier or more of the tension was released. [14]

The sample size of the study was calculated 50 using OpenEpi. [12] Data analysis was performed at SPSS version 20. The normality of data was checked by using Shapiro-Wilk test. At baseline and end values between the groups Mann-Whitney's test was applied for non-normal data whereas for pre-and post-values comparison within the groups Wilcoxon test was applied for non-normal data.

RESULTS

The study has been designed and reported in accordance to the consort guidelines (15). The final sample

was composed of 50 subjects, randomly allocated 25 participants in experimental group and 25 in control group. All patients received allocated intervention. Loss of follow-up in experimental group was 3 and in control group it was 4. (Figure.no:1)

Percentage of active, latent, L1 and L2 myofascial trigger points in control and experimental groups are shown in detail in (Figure no-3 and 4) respectively.

In the baseline comparison between the two groups, parametric test was applied. Pain pressure threshold showed no significant difference in first pre-session with the P value 0.267. Mean of experimental group and control group is shown in the (Table.no:1) In the baseline comparison between the two groups, non-parametric test was applied. PML, VAS and ODI showed statistically no significant difference. Paraspinal muscle length in first pre-session had a P value of 0.659 while the VAS P value was 0.236 and ODI in first pre-session P value was 0.059. Mean rank and IQR in experimental and control group is shown in (Table no-1)

Post intervention comparison between the two groups the non-parametric test was applied. The PPT and VAS show statistically significant difference and ODI had no significant difference. PPT in last session mean rank was 28.32 in experimental group and in control group mean rank were 15.38 with IQR 22 (3) having P value 0.001.

VAS in last session mean rank was 14.43 in experimental group and in control group, the mean rank was 29.93 with IQR 1 (2) having P value of 0.000. ODI in last session mean rank was 19.00 in experimental group and in control group mean rank was 25.14 with IQR 4.4 (20.8) having P value 0.105. At the end, for comparison between the two groups, Independent T test was applied. PML in last session shows no significant difference with the mean 17.1±3.04 in experimental group. And the mean of control

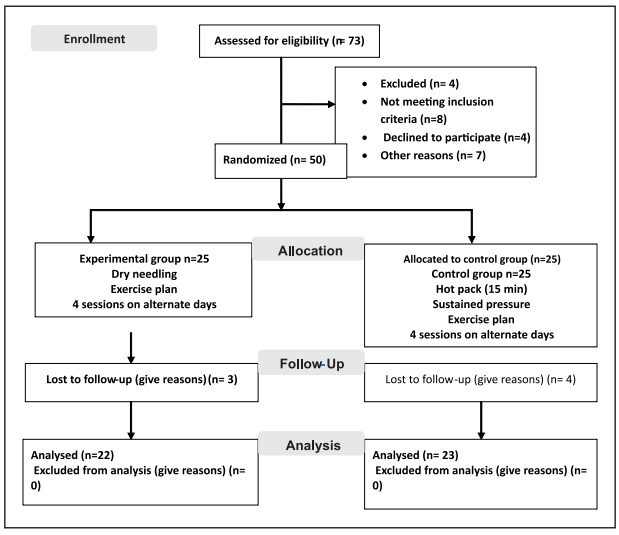

Fig 1: Consort flow chart

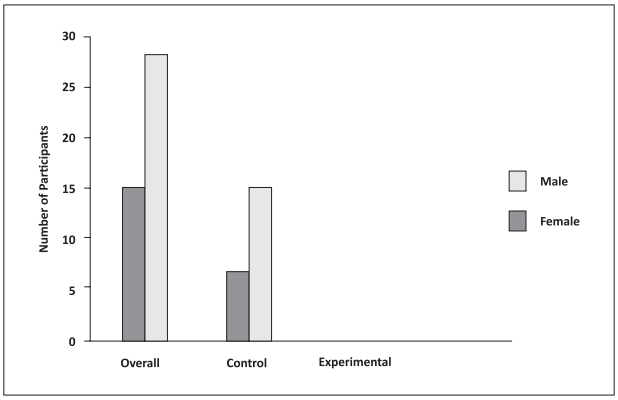

Fig 2: Number of participants according to gender in two groups

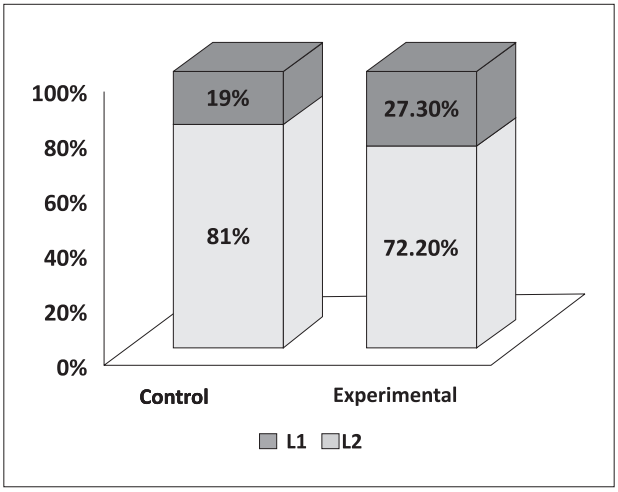

Fig 3: Percentage of Trigger point L1 and L2 in two groups

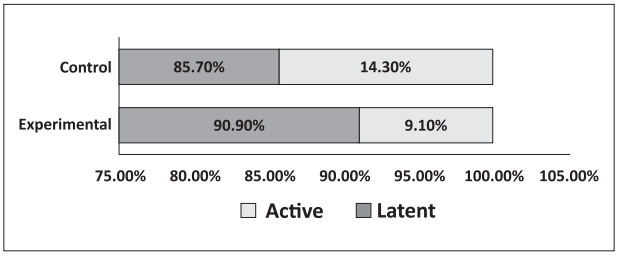

Fig 4: percentage of active and latent trigger points in two groups

group was 18.2±1.76 with the P value 0.140. The comparison of pre-and post-values of PPT, PML, VAS and ODI in control group showed statistically significant difference. Pain pressure threshold, para spinal muscle length and VAS have P-value < 0.01.

DISCUSSION

Trigger points are distinct, focal, hyperirritable spots located in a taut band of skeletal muscle. They produce pain locally and in a referred pattern and often accompany chronic musculoskeletal disorders. [16] A major number of patients having low back pain has MTrPs as

Table 1: Changes in hematological parameters in study sample (n=101)

Variables	Groups	Mean ±SD	P Value	
Pain pressure threshold (IIb)	Control	13.4±2.30	0.267	
	Experimental	14.2±2.33		
Variable	Group	Mean rank	IQR	P Value
Paraspinal muscle length (inches)	Experimental	21.18	20(3)	0.659
	Control	22.86		
Visual analogue scale	Experimental	24.07	7(1)	.236
	Control	19.83		
Oswestry disability index	Experimental	25.52	48.8(28.9)	0.059
	Control	18.31		

a common source of pain in lumbar paraspinal muscles. [17] In 2015, Shane L. Koppenhaver et al. conducted a research to find out the post needling intervention changes in lumbar Multifidus muscle function and pain sensitivity in patient responders versus non-responders. Sixty-six patients having low back pain ultrasound measurements and PPT with Algometer of lumbar Multifidus muscle were measured at pre-session, immediately after dry needling intervention, and after one week. ODI was also measured in these patients. It was concluded that the pain sensitivity was significantly decreased (mention p-value) one week post dry needling sessions and improvement in ODI scoring was observed. The results of this study support the outcomes of our study in relations to ODI and PPT improvement in experimental group post session. [18]

In 2014, María J. Mejuto-Vázquez, PT et al. conducted a research study on short term outcomes in patient with acute neck pain having MTrPS after dry needling in terms of nociceptive sensitivity and cervical ROM. PPT, cervical ROM and NPRS were recorded at 10 minutes and 1 week after intervention. They concluded that single session of trigger point dry needling group provides short term outcomes with improved PPT and cervical ROM and decreased NPRS. The previous study supports the result of this study as after dry needling session, many of patients after single session of TrP dry needling had improved PPT and decreased VAS. [19]

In 2016 Muhammad sharifullah et al. conducted a research study in RG hospital of Pakistan. The researchers compared the effects of sustained pressure and ischemic pressure in improving chronic myofascial pain. After getting 8 sessions of ischemic compression and sustained pressure by cases and controls, NPRS readings showed that both groups had improved pain symptoms but there was no noteworthy advancement in pain relief among sustained pressure and ischemic pressure groups. The results of this study support the findings of the current study as in control group, after taking 4 sessions of sustained pressure along with conservative management, there was decrease in VAS in majority of patients. [20]

CONCLUSION

It is concluded that both sustained pressure and dry needling are effective treatment options for treatment of myofascial trigger points in lumbar paraspinal muscle. Dry needling decreases the pain as shown on the value of pain pressure threshold and visual analogue scale. However, Dry needling does not show any significant improvement in patient disability and lumbar paraspinal muscle length.

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AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under

Zia A:	Manuscript writing, concept, Study Design
Sajjad AG:	Data collection, Writing
Hafeez A:	Manuscript writing, Study Design
Altaf S:	Overall supervision, and approval of the final version.
Khan N:	Data collection, helping in manuscript writing
Malik RJ:	Data collection, helping in manuscript writing

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

ORIGINAL ARTICLE

HISTOLOGICAL PATTERN OF NON-DIABETIC RENAL DISEASE IN TYPE 2 DIABETES MELLITUS. A STUDY IN A TERTIARY CARE HOSPITAL

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ABSTRACT

OBJECTIVE: To determine the histological pattern of non-diabetic renal disease in type 2 diabetes mellitus.

MATERIAL AND METHODS: This descriptive, cross-sectional study was conducted in the Nephrology department MTI Lady Reading Hospital Peshawar from January 2018 to January 2021. All type 2 diabetic patients with normal fundi were included in the study irrespective of time duration. A total of 30 patients were registered. Their biodata was entered in a prescribed proforma. Those having normal fundi were included in the study and were then exposed to renal biopsy. Those patients having diabetic retinal changes were excluded from the study.

RESULTS: Out of 30 patients, males were 20 and females were 10 with a ratio of 2:1 with a mean age of 55.5±13.3SD years. Pure diabetic nephropathy (DN) was noted in 9 (30%) cases, Non-Diabetic Renal Disease (NDRD) in 13 (43.3%) cases, and NDRD on DN in 8 (26.7%) cases. Among the Non-Diabetic Renal Disease (NDRD), Membranous Glomerulonephritis (MGN) was present in 9 (30%) cases, Acute Tubular Necrosis (ATN) in 5 (16.6%) cases, Focal Segmental Glomerulosclerosis (FSGN) in 4 (13.33%.) cases, Mesangiocapillary Glomerulonephritis (MCGN) in 2 (6.7%) cases and Hemolytic Uremic Syndrome (HUS) in 1 (3.3%) cases.

CONCLUSION: It was concluded from the study that the absence of diabetic retinopathy does not exclude diabetic nephropathy. Renal biopsy should be done in all patients with type 2 DM irrespective of time duration especially with normal fundi and atypical renal involvement.

KEYWORDS: Renal biopsy, Fundoscopy, Non-diabetic renal disease, Glomerulonephritis

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INTRODUCTION

Diabetic nephropathy (DN) has been reported as the leading cause of chronic kidney diseases and End-Stage Renal Disease (ESRD). [1, 2] Diabetes has been reported as one of the most important causes of ESRD in Europe and Asia, contributing to 20–30% of the incident ESRD patients in Europe and up to 40–55% in certain parts of Asia. [3-6]

The development of chronic complications of diabetes is closely related to diabetic control. Micro and macrovascular complications of diabetes can result in significant morbidity and mortality. [7] The diagnosis of DN is almost always based on clinical grounds in type 1 diabetes but not in those with type 2 diabetes mellitus. [8] Diabetic retinopathy is a screening and diagnostic clinical finding for DN in type 2 diabetic patients. Proliferative diabetic retinopathy may be a highly specific indicator for diabetic nephropathy. [9] Non-diabetic renal diseases (NDRD) either isolated or superimposed on an underlying DN, have been reported. The prevalence of biopsy-proven NDRD in patients with diabetes varies from 10–85% among different reports. [10-13] These differences may be due to set criteria or the populations being studied.[14, 15]

Better kidney survival has been reported in the early diagnosis and appropriate therapy of patients with non-diabetic renal disease. [16] The indication of renal biopsy in patients with type 2 DM in absence of diabetic retinopathy has been reported, in atypical clinical features of renal involvement with short duration, acute onset of nephrotic syndrome, proteinuria with active urine sediment, and acute kidney injury of unknown cause. [17, 18]

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Treatment of NDRD is completely different from DN. Immunosuppressive therapy is the mainstay of the treatment in NDRD apart from angiotensin-converting enzyme inhibitors or angiotensin receptor blockers and statins. Thus, it is important to diagnose NDRD very early and for that, kidney biopsy is necessary to confirm the diagnosis. This study was aimed to determine the frequency of NDRD with or without DN in type 2 DM patients who have an atypical presentation of diabetic renal involvement. NDRD is defined as a kidney disease that is not associated with diabetes mellitus and with the absence of changes in the target organs (retinopathy) caused by long-term diabetes mellitus.

MATERIALS AND METHODS

This descriptive, cross-sectional study was carried out in the Nephrology Department, Lady Reading Hospital Peshawar from January 2018 to January 2021. This study comprised of 30 patients having nephropathy with a history of type 2 diabetes mellitus at the time of diagnosis irrespective of duration. Male and female patients of all age groups were included. Renal biopsy was performed in all those cases who had unexplained rapidly increasing proteinuria, active urine sediment and rapidly rising creatinine, and proteinuria with rising creatinine and renal involvement with the normal funduscopic examination. Fundoscopy was done and fundal photographs were taken of all patients. Patients having type 1 diabetes mellitus and those who have diabetic retinopathy were excluded from the study. Institutional ethical approval was granted for this research work.

Written consent was taken from all patients and biodata was entered on prescribed proforma. Variables were entered in SPSS 20.0. Variables like name, age, sex, duration and type of diabetes, proteinuria, urea and creatinine, ultrasound, Fundoscopy, and renal biopsy findings were recorded. Fundoscopy findings were broadly categorized into normal, non-proliferative, and proliferative diabetic retinopathy. All renal biopsies were sent to Ziauddin Hospital Karachi for histopathology and immunofluorescence.

RESULTS

The total number of patients was 30. Male were 20 (70%) while females were 10 (30%). The age range was 25 years to 88 years with a mean age of 55.5±13.3SD (table 1). Pure Diabetic Nephropathy (DN) was present in 9 (30%) cases, NDRD on DN in 8 (26.69%) cases, and NDRD in 13 (43.4%) cases (Table 2). The most common histological pattern was membranous GN (09 cases, 30%) followed by ATN (05 cases, 16.6%), FSGS (4 cases, 13.33%), and Keimel Stiel Lesions were seen in 9 (30%) patients. MSGN was present in 2 (6.6%) cases and HUS in 1 (3.4%) cases (Table 3). Different variables were correlated with nephrotic range proteinuria and a p-value was calculated. A P-value less than 0.05 was considered significant (table 4).

Table 1: Age Distribution

	N	Minimum	Maximum	Mean	Std. Deviation
Age	30	25.00	83.00	55.5000	13.27105

Table 2: Prevalence of NDRD with or without DN

Variables	Frequency	Percent
DN	9	30.0
NDRD	13	43.3
NDRD on DN	8	26.7
Total	30	100.0

Table 3: Renal Biopsy Findings

Variables	Frequency	Percent
Acute tubular necrosis	5	16.7
Diabetic nephropathy	9	30.0
Focal Segmental Glomerulosclerosis	4	13.3
Hemolytic uremic syndrome	1	3.3
Mesangiocapillary glomerulonephritis	2	6.7
Membranous glomerulonephritis	9	30
Total	30	100

Table 4: Correlation of variables with Proteinuria >3gm

Variable	P-value
DN (n=09)	0.031*
NDRD (n=13)	0.004*
NDRD on DN (n=08)	0.001*
Duration of Diabetes (years)	0.335
Gender of Patients	0.770
Age of Patient (years)	0.717
Hypertension	0.783
Level of Creatinine	0.284

DISCUSSION

Diabetes Mellitus is one of the fastest-growing chronic diseases worldwide. [27] Diabetic nephropathy is the leading cause of ESRD requiring dialysis. [19] Although patients with T2DM often end up in DN, but they can also experience other renal diseases, unrelated to diabetes and known as NDRD.[11] In this study, three groups were made. The aim was to determine the prevalence of DN, NDRD and NDRD superimposed on DN in type 2 diabetic patients with atypical renal involvement. In the present study, the mean age was 55.5 years ±13.27 SD with male (n=20) outnumbering the female (n=10) with male to fe-

male ratio of 2:1. Unnikrishnan et al, covering the south Indian population reported the average age of patients as 51 ± 12 years. [20] Mak et al reported average age was 57 ± 1.8 years in patients having DN and 50 ± 1.9 years in patients having mixed lesions in their study. [21] Yip- Boon Chong et al also showed a mean age of 53.8 ± 9.7 years with male predominance. [22] Thus, our study was similar to other studies in terms of age and gender.

In our study, NDRD with 13 cases (43.3%) was the most common entity followed by DN with 9 cases (30%) and NDRD on DN with 8 cases (26.7%). In this regard, our study has similarities with a study conducted by Prakash J et al in which NDRD was 41.9%, DN 38.7%, and NDRD superimposed on DN 19.4%. [23]

The most common pathology in the NDRD group was Membranous GN with 9 (30%) cases followed by FSGS with 04 cases (13.33%). In the DN+NDRD group, ATN was the most common entity. This finding is correlating with the results of other studies. [17, 18, 24, 25] Another Iranian study conducted by Tayebeh et al also favors the same finding. [26] while another study by Pham TT contradicts our study in which FSGS was the most entity. [25]

In this study, the duration of diabetes before the biopsy was significantly shorter among the NDRD patients. However, the lack of diabetic retinopathy was the only independent predictor of NDRD. The literature review shows that in many studies, the short duration of diabetes was an indicator of NDRD.[14, 16] In our study, the mean duration of diabetes mellitus was 11±7.12 SD years. In contrast, Mak SK et al mentioned in their study that DN could not be distinguished from NDRD by the presence of diabetic retinopathy, age of onset, and duration of diabetes. [21] This correlates with our findings as well. We found that diabetic retinopathy was absent among all groups. Similarly, the NDRD and DN groups of patients were having a higher rate of proteinuria and were frankly nephrotic. The majority of the Patients with NDRD and DN were having acute kidney injury. Similar findings were also reported by Taybeh et al. [26] As this is a single-center study on a small population of patients, so care should be taken to generalize the results on all diabetic populations. Large center studies involving different institutions need to be carried out for this purpose.

CONCLUSION

On basis of our study, it is suggested that routine presumption of type 2 diabetes as the cause of diabetic nephropathy may not be correct because NDRD or mixed lesions may develop in these patients as seen in our study. Therefore, in selected patients with unusual renal involvement, renal biopsy should always be considered because disease-specific therapies may prolong renal survival.

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AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under

Muhammad N: Concept/ Idea, Literature, review, Drafting & Final Review

Khan Z: Concept/ Idea, Analysis & Interpretation of Data, References

Khan MW: Manuscript Writing, Literature review, Analysis & Interpretation of Data

Muhammad S: Manuscript Writing, Literature review, Analysis & Interpretation of Data

Ikram M: Concept/idea, Data Collection

Ikram S: Concept/idea, Literature review, Drafting & Final Review

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

ORIGINAL ARTICLE

CHARACTERIZATION OF PREVALENT ECHINOCOCCUS GRANULOSUS GENOTYPES THROUGH MODIFIED PCR-RFLP TECHNIQUE

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ABSTRACT

Objective: We aimed to investigate the genetic diversity of *echinococcus granulosus* using a modified Polymerase Chain Reaction-Restriction Fragment Length Polymorphism (PCR-RFLP) based assay in the infected population.

Materials and methods A total of 18 human hydatid cyst samples were collected from various hospitals of Southern Punjab and Islamabad Capital Territory region of Pakistan. Extracted DNA was used for PCR amplification of mitochondrial NADH dehydrogenase subunit 1 (Nad1) gene followed by sequencing and phylogenetic analysis using Molecular Evolutionary Genetics Analysis (MEGA) Software. The entire sequences were fed into NEBcutter V2.0 to select a single restriction enzyme followed by invitro confirmation through PCR-RFLP.

Results: Amplification on the Nad1 gene was observed in 100% of the samples processed. The Basic Local Alignment Tool (BLAST) and phylogenetic tree analysis revealed 83.3% *E. granulosus* (G1-G3 genotypes), 11.1% *E. multilocularis* and 5.6% *E. Canadensis* (G6 genotype). The use of the *BfaI* enzyme in PCR-RFLP analysis revealed that all of the 18 samples were assigned consecutive genotypes as observed in the sequencing.

Conclusion: The current study concluded that the *BfaI* enzyme could be used for the genotypic analysis of echinococcosis in developing and frequently affected countries. It will be a cost-effective and easy technique compared to sequencing, which will aid in developing novel therapeutic and control strategies for the parasite.

Key words: *echinococcus granulosus,* Polymerase Chain Reaction, Restriction Fragment Length Polymorphism

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INTRODUCTION

Cystic echinococcosis (CE) is an important socio-economic zoonotic infection caused by canid tapeworm Echinococcus granulosus. The parasite requires two hosts for its life cycle completion: a definitive host (canid) and an intermediate host like (herbivores) and humans. The intermediate hosts get infected through the fecal-oral route by ingesting the parasite eggs in the feces of the definitive host. The eggs hatch to release oncospheres (hexacanth embryos), which migrate to blood vessels through the intestinal wall and infect various organs like the lung and liver, developing fluid-filled cysts (often 3~10 cm in diameter). Human cystic echinococcosis is a chronic infection with an asymptomatic phase (months to years) followed by acute clinical signs like pain or swelling due to the cyst pressure exerted on surrounding parenchymal tissues. [1-3] The clinical manifestation depends upon the size, number, affected organ, and localization of the cysts. The disease can be life-threatening when cysts rupture and their contents (fluid, protoscoleces, and brood capsules) spill into the peritoneal cavity, resulting in anaphylactic shock and establishment of secondary CE. Due to its zoonotic nature, CE can affect millions of humans and livestock population responsible for huge financial and health losses due to the condemnation of infected livers and lungs from livestock animals and also difficult to diagnose and treat in humans. [4, 5]

Cystic echinococcosis is reported from the human and livestock population and is endemic in various parts

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of Pakistan. [6-9] Globally, 10 distinct genotypes (G1-G10) of E. granulosus sensu lato have been defined based on mitochondrial DNA studies among various countries like Africa, Asia, Australia, Europe, South America, and the USA. [10-18] The genetic characterization of E. granulosus plays a central role in understanding transmission patterns of the parasites between definitive hosts and intermediate mammalian hosts/humans as well as diagnosis and control of CE. [19-21] Various DNA-based tools, particularly PCR and sequencing of nuclear and mitochondrial gene regions, have been applied to the genetic classification of echinococcus species and genotypes. [22-24] The PCR-RFLP-based genotypic technique revealed various species of CE. However, there is a need for a novel restriction enzyme that can be simultaneously used to discriminate various species of echinococcus granulosus. Since genotypic identification of echinococcus species is imperative for devising strategies for its control, the current study used a single restriction enzyme BfaI for genotypic characterization followed by verification with currently recognized genotypes through sequencing and phylogenetic analysis.

MATERIALS AND METHODS

The current study was performed from September 2018 to September 2019 at Molecular Virology Laboratory (MVL), Department of Biosciences, COMSATS University Islamabad. This study was reviewed and approved by the Ethical Approval Committee of COMSATS University, Islamabad, under Reference No. CUI-Reg/Notif. 2255/19/2661. A total of 18 hydatid cyst samples removed via surgery were collected from various hospitals of District Dera Ghazi Khan and Rajanpur and transferred to MVL for processing. The cyst contents (fluid and protoscoleces) were aspirated aseptically into sterile test tubes (McManus and Symth, 1978), followed by mild spinning by centrifugation at 3000 rpm for l0 minutes at room temperature. The supernatant was discarded. The residue was taken by Pasture pipette and placed on a microscopic slide and examined under the microscope (40X) for the presence of protoscoleces.

NUCLEIC ACID EXTRACTION

Total nucleic acid was extracted from Cyst fluid (protoscoleces) and the germinal layer using DNeasy Blood and Fluid Kit (Qiagen, Hilden, Germany) and phenol-chloroform method as described earlier. Extracted DNA concentration was determined using a NanoDrop spectrophotometer (Thermo Scientific, USA) and then stored at -20C until further used for PCR amplification.

MOLECULAR CHARACTERIZATION

Molecular characterization of E. granulosus was performed using mitochondrial Nad1 gene fragment as described earlier (Kim et al., 2017). PCR amplified products were separated on 2% agarose gel electrophoresis, pre-stained with ethidium bromide, followed by UV transilluminator visualization according to their fragment size. Sequencing and phylogenetic analyses: PCR products were sequenced in both directions using Forward primer (Nad1-F[A(G/A)(A/T) TTCGTAAGGG(G/C)CCTAATA) and a Reverse primer Nad1-R ((A/T)CC(A/T)CTAAC(T/C) AATTCACTTTC) (Macrogen Inc., Seoul, South Korea) and read by Chromas software (Technelysium Pty Ltd., Queensland, Australia). The sequences were aligned and assembled using DNASIS MAX (version 3.0; Hitachi, Yokohama, Japan) and BLAST searched (http://blast.ncbi.nlm.nih.gov) in the GenBank database. Our sequences were aligned with reference sequences for each genotype in MEGA software (www.megasoftware.net). A phylogenetic tree was created using Maximum Likelihood algorithms with evolutionary distances calculated by the Kimura-2 parameter method and a bootstrap value of 1000. Polymerase Chain Reaction-Restriction Fragment Length Polymorphism (PCR-RFLP): All sequences were fed into NEBcutter online server (http://nc2.neb.com/NEBcutter2/), and the BfaI restriction enzyme was selected for in-vitro analysis. The entire PCR product of the Nad1 gene was digested through the BfaI enzyme (Biolabs Inc) for 3-4 hours at 37^{0}C followed by 2% gel electrophoresis and visualization on a UV transilluminator.

RESULTS

Molecular Characterization of Echinococcosis

The extracted genomic DNA of the entire 18 hydatid cyst samples were amplified through Echinococcal mitochondrial gene Nad 1 giving a 530bp amplified band (Figure 1) Sequencing and Phylogenetic Analysis: Sequencing and phylogenetic analysis of the entire samples showed 83.3% (15/18) E. granulosus senso stricto (G1-G3 genotype) followed by E. multilocularis 11.1% (2/18) and 5.6% (1/18) E. canadensis (G6 genotype).

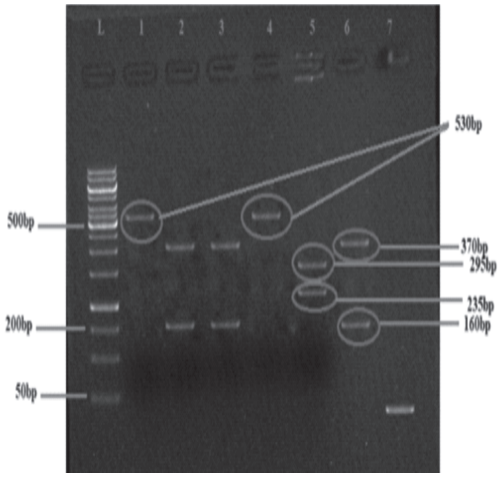

Fig 1: Agarose gel electrophoretogram of PCR product of NAD1 gene and PCR-RFLP of unidentified Echinococcus sp.

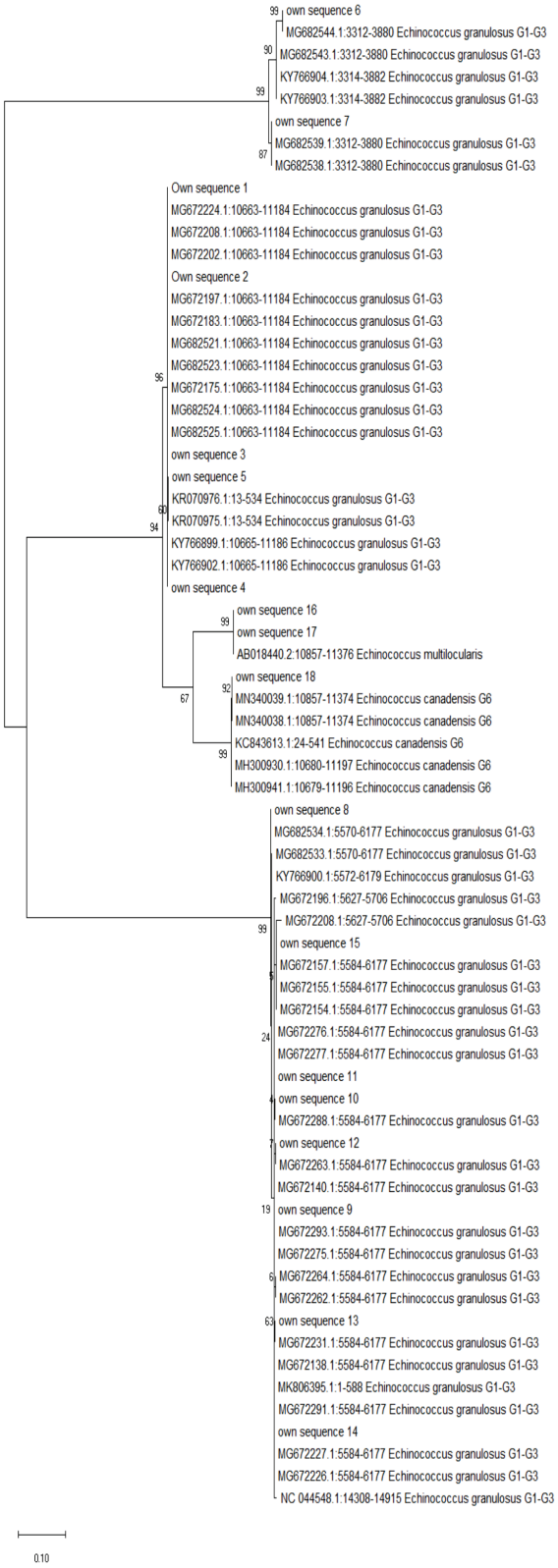

Fig 2:Maximum Likelihood Phylogenetic Tree showing E. granulosus (G1-G3), E. canadensis (G6), and E. multilocularis genotypes based on nucleotide sequences of the NAD1 gene.

PCR-RFLP ANALYSIS

Upon digestion, through BfaI enzyme PCR amplified product was restricted at two sites resulting in band sizes of 256bp, 108bp, and 166bp. Sequencing of the resultant restriction digested bands showed genotype G1-G3 E. granulosus (83.3%), followed by E. multilocularis 11.1% and E. canadensis (G6) 5.6% confirmed by the phylogenetic tree (Figure 2)

DISCUSSION

Echinococcosis is a neglected, zoonotic public health concern of the modern era infecting both humans and animals. Echinococcosis has a complex etiology attributed to ten diverse species of Echinococcus granulosus Senso stricto (WHO, 2021). Two mitochondrial genes, cytochrome C oxidase (COX) and NADH1 dehydrogenase (NAD1), are generally used for the classification species. [25] Various techniques are used for genotypic isolation of the infective or prevalent Echinococcal species in humans, including PCR-RFLP and amplified gene sequencing followed by phylogenetic analysis. Various species were reported from Pakistan, including E. granulosus. (G1-G3) and E. Canadensis (G6/G7), E. multilocularis, through PCR-RFLP; however, some species like E. equinus (G4) and E. ortleppi (G5) are recently reported through sequencing and subsequent phylogenetic analysis. [6-8]

Most of the genotypic studies rely on sequencing, BLAST, and phylogenetic resemblance; however, besides its accuracy, sensitivity, and specificity, the lack of resources and time consumption constrain the developing world towards old techniques like PCR-RFLP and genotypic specific ELISA. [6, 24] The majority of sequencing data reported 10 different Echinococcus granulosus species (G1 to G10) and E. multilocularus all over the world, including Pakistan from the human and animal population. Similarly, the current study revealed that the majority of the human infection was caused by E. granulosus (G1-G3) followed by E. multilocularis and E. Canadensis (G6). [6-9] E. granulosus sensu stricto (G1-G3) is the most prevalent species in the human population. [26-28] On the broad spectrum, genotype G1 is the most prevalent genotype in the world, which might be due to a wide intermediate host range that facilitates higher circulation in the environment. [28-37] A possible reason describing the prevalence of G1-G3 species in the current study could be the animal trade among the neighboring countries. It thus promotes the genotype distribution from one country to another. [31]

Polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) use various restriction enzyme for selected mitochondrial genes (rrnL, large subunit of ribosomal RNA) containing a species-specific SspI restriction site for the differentiation among E. granulosus and E. multilocularis from Pakistan while other reports identify 10 genotypes (G1-G10) by using a variety

of restriction enzymes for COX1 and NAD1 mitochondrial genes however unable to separate G6/7 genotype. Another study used three different restriction enzymes for ITS1 and rDNA and reported two species of echinococcus granulosus. [38] Various reports revealed that there a single restriction enzyme cannot be enough for genotyping through PCR-RFLP. However, a recent report suggested that using the restriction enzyme BfaI might differentiate various echinococcus genotypes effectively. In agreement with findings from earlier reports, the current study used the NAD1 sequence and fed it into NEBcutter online server, which effectively distinguished the reported species through BLAST and phylogenetic analysis. In-vitro confirmation revealed G1-G3, G6, and E. multilocularis by using BfaI restriction enzyme through PCR-RFLP.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding authors.

ETHICS STATEMENT

The study was approved by the Ethical Approval Committee of COMSATS University, Islamabad under Reference No. CUI-Reg/Notif. 2255/19/2661.

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AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under

Basharat N:	Concept/ Idea, Literature, review, Drafting & Final Review
Ansari SH:	Analysis & Interpretation of Data, References
Khan J:	Manuscript Writing, Literature review, Analysis & Interpretation of Data
Gul A:	Concept/idea, Data Collection
Ali L:	Concept/idea, Literature review

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

ORIGINAL ARTICLE

THE EFFECTIVENESS OF CLOSED REDUCTION OF SUPRACONDYLAR FRACTURE OF THE HUMERUS WITH NEUROVASCULAR INJURY IN TERMS OF THE NEED FOR EXPLORATION IN CHILDREN

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ABSTRACT

Objective: To determine the effectiveness of closed reduction of supracondylar fracture of the humerus in children with neurovascular injury in terms of the need for exploration.

Material and Methods: This prospective observational study was conducted at the department of Orthopedic Khyber Teaching Hospital Peshawar from July 2020 till July 2021. Children with supracondylar fracture (Gartland type II and III) of the humerus were included irrespective of neurovascular injury. Data was analyzed using SPSS. Mean and standard deviation was used for quantitative data. Frequency and percentages were used for qualitative data. Shapiro Wilk's test was done to find the normality of the data.

Results: The mean age of the 65 children with Gartland type 3 closed fractures was 7 years (± 1.5) years. The male to female ratio was 1:0.4 with 45 males and 20 female patients. The right side was involved in 28 (43%) while left sides in 37(57%) patients. At presentation, 40 patients (61%) had no signs of neurovascular involvement while 25 patients (39%) had signs and symptoms of various nerve injuries and 6 patients had absent radial pulse but with well perfused, pink hand. Of these 25 patients, only 2 patients had combined neurovascular compromise not responding to closed reduction and needed urgent exploration while the remaining 23 were managed conservatively with closed reduction

Conclusion: This study concludes that closed reduction should be done in patients with isolated nerve injury or vascular injury with pink hand and adequate capillary refill while in case of combined nerve and vascular injury not responding to closed reduction, urgent exploration should be considered.

Key Words: Supracondylar fracture of the humerus, Neurovascular injuries, Median nerve, Ulnar nerve, Radial nerve, Gartland classification.

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INTRODUCTION

The neurological and vascular injury in displaced supracondylar fracture of humerus in children is reported in 10 to 20% of cases.[1, 2] The Early recognition of ischemic injury is a matter of great concern for the reversibility of damage, depending upon the duration of the ischemia.[3] The vascularity of the limb in Gartland Type-III injury needs due attention for its survival.[4] The brachial artery injury has been reported in approximately 11% of cases of supracondylar fractures.[5, 6]

There is no dispute in urgent exploration in the case of vascular comprise in supracondylar fracture with pulseless, cool, and white hand.[7] However, the controversy remains there when there is pulseless and pink hand in displaced supracondylar fracture of humerus and several authors have suggested a conservative approach or delayed surgery.[8] Most of the surgeons initially manage such types of injuries with urgent close reduction and K-wire fixation. Mostly, the radial pulse will return immediately.[9] In a study of the British Society of Orthopedic surgery, 60%

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favored observation if the hand remains pulseless after k-wire fixation, whereas 16% favored exploring the vessel immediately and the remainder would call for a vascular surgeon opinion.[10] The neurological injuries may coexist with vascular injuries. The median and anterior interosseous nerves are commonly injured in extension type of supracondylar fracture especially when the distal fragment is displaced posteriorly and laterally.[11, 12] In some studies, radial nerve injuries are reported as the most common nerve injuries followed by median and ulnar nerve.[13] In most of the studies, complete recovery of the nerve function has been reported without the need for exploration which shows that the injury may be partial (neuropraxia).[11, 12] In case of coexisting vascular and median nerve injury, the chances of nerve recovery would be unlikely with conservative treatment, so in such a situation early exploration is required from an anteromedial approach to see kinking or rupture of the vessel and median nerve.[14] The radial pulse will return if the vessel is in spasm or completely obstructed by thrombosis / intimal tear or is trapped at the fracture site. In these cases, the return of radial pulse is due to dilatation of collateral circulation around the elbow.[5]

Table 1: Basic Demographics of the study

Mean Age of patients	**7 years ± 1.5 years**
Distribution with respect to Gender	
Male	45
Female	20
Male to female ratio	1:0.44
Distribution with respect to side involvement	
Right Side	**28**
Left Side	**37**
Distribution with respect to neurovascular compromise	
Present	**25**
Absent	**40**

The local literature seems to be deficient with no appropriate recommendations for dealing with neurovascular compromise in supracondylar humeral fracture. This study aimed to determine the role of closed reduction and its outcomes in supracondylar humeral fracture with neurovascular compromise in terms of the need for exploration in children.

MATERIALS AND METHODS

This prospective observational study was conducted at the Department of Orthopedic Khyber Teaching Hospital Peshawar from July 2020 till July 2021. The inclusion criteria was displaced (Gartland Type II and III) supracondylar fractures of the humerus in children presented with or without neurovascular injury prior to an attempt of close or open reduction. The exclusion criteria was fracture treated elsewhere and supracondylar fracture with pulseless, cool, and white hand. The fractures were classified according to Gartland classification and proper clinical examination was performed before any sort of treatment to find out any neurovascular compromise. The patients with isolated vascular and nerve injury were treated with closed reduction while patients with combined neurovascular injury underwent surgical exploration. The neurovascular status was assessed upto 3 days of the above-mentioned intervention and then after 3 months.

RESULTS

A total of 65 children with Gartland type 3 closed extension type supracondylar fractures were included in the study, the basic demographics of which are discussed in Table 1.

Out of these 65 patients, only 25 had signs and symptoms of neurovascular compromise which are discussed in Table 2.

Table 2: Details of neurovascular compromise

Parameters	**Number of patients**	**Status at 3rd day**	**Status 3 months**	**Need for exploration**
Only Vascular compromise	6 Absent radial pulse	Pulse reappeared in 2 patients after closed reduction	in 4 patients pulse reappeared after 3 months of closed reduction with normal capillary refill	None
Only Nerve compromise	11 Anterior interosseous nerve 8 Median Nerve 6 Radial Nerve 0 Ulnar Nerve	Neuropraxia in all cases after closed reduction	Normal status after three months of closed reduction	None
Combined neurovascular compromise	2 Radial artery and median nerve involved	Closed reduction failed Radial pulse reappeared at 48 hours after exploration	Closed reduction failed Median nerve function reappeared after 3 months of open reduction	Openly explored

DISCUSSION

The neurovascular injuries in supracondylar fractures of the humerus in children are common in Gartland type III extension type fractures.[15] There is controversy regarding the management of pulseless but perfused hand after close reduction. Some authors opt for conservative management while other favor early exploration.[16]

In the literature, there are different frequencies of various nerve injuries in supracondylar fractures of the humerus in children. In one study, the nerve injuries occurred in 13.3% of patients, with median nerve 58.9% followed by radial 26.4% and ulnar nerve injuries 14.7%, combined nerve and vascular injury occurred in 2.9%. [11] In another study conducted in the U.S.A, nerve injuries were reported in 19 (9.5%) cases out of 200 cases with acute type III extension type Supracondylar fractures.[17] The percentage of nerve injuries in our study was 38%. There was 44% anterior interosseus nerve involment, 32% median nerve while 24% radial nerve and no ulnar nerve. On the other hand, percentage of the vascular injury in our study was 24%. The percentage of combined neurovascular injury was 8%.

We managed six cases with absent pulse by closed reduction and percutaneous pinning without exploring the brachial artery. The logic behind this approach was that in well-perfused pulseless hands the radial pulse usually appears following relaxation from vascular spasm. Likewise, strong collateral circulation also develops around children's elbow. [5] In 2 cases having both an absent radial pulse and median nerve injury, the brachial artery and nerve were explored through an anteromedial approach. The brachial artery and median nerve were found entrapped between fracture fragments, both were released and fracture fixed with cross k-wires. In both cases, pulse reappeared after 72 hours and median nerve started functioning within 3 months.

In our study, we also found that the median nerve is most commonly injured in displaced supracondylar humerus fractured in children followed by radial and ulnar nerve. In other studies, radial nerve injury is most commonly injured followed by median and ulnar nerve. [13]

Moreover, we noted that in supracondylar fractures with posteromedial displacement the radial nerve got injured due to anterolateral pressure of proximal humeral fragment, while the median nerve and brachial artery injuries occurred in posterolaterally displaced fractures due to anteriomedial pressure of proximal fragment as reported by other authors.[11] Diagnosis of fracture displacement pattern provides a clue toward clinical examination for nerve injury assessment. In children, it is very difficult to assess nerve injury but one can get some clue of nerve injury by thumb moments.

Due to the limited number of participants in the study, it is difficult to generalize the results. Further large scale multicenter studies of this kind are needed to improve our understanding and strengthen the guidelines.

CONCLUSION

This study concludes that closed reduction should be performed in children with isolated nerve injury or vascular injury with pink hand and adequate capillary refill while in case of combined nerve and vascular injury not responding to closed reduction, urgent exploration should be seeked.

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Khan MY: Study design, overall supervision, and approval of the final version.

Khan MS: Manuscript writing, concept, Study Design

Khan MAJ: Data collection, helping in manuscript writing

Sajjad A: Data collection

Khan MK: Study design, overall supervision

Shoaib F: Manuscript writing

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

SWYER SYNDROME WITH A GERM CELL TUMOUR

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ABSTRACT

Objective: A 23-year-old patient with primary amenorrhea and female external phenotype presented to the outpatient department of Mercy Teaching Hospital, Peshawar. On clinical examination, she was tall with under developed secondary sexual characteristics. Laboratory/ radiological investigations revealed Swyer syndrome. Karyotyping showed XY chromosomal pattern. On imaging, a left huge adnexal mass, 16x12cm with multiple solid and cystic areas, small infantile uterus and right streak ovary was detected. Alkaline phosphatase, LH and FSH levels were raised. Laparotomy followed by left salpingoophrectomy was done. Intra-operatively, there was a small infantile uterus and right streak ovary and right normal looking fallopian tube with no ascites, visceromegaly and enlarged abdominal lymph nodes. Histopathology revealed dysgerminoma.

Conclusion: Swyer syndrome also known as pure gonadal dysgenesis is a rare form of genetic disorder. Clinically, the patient has female external phenotype and XY chromosomal pattern. Early investigations and radiological imaging help in the proper diagnosis. Prophylactic gonadectomy reduces the risk of developing germ cell tumors.

Key words: Swyer syndrome, Germ cell tumors, Pure gonadal dysgenesis.

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CASE REPORT

A 23-year-old patient presented to Mercy teaching hospital, Peshawar with female external phenotype, primary amenorrhea and pain lower abdomen. She had no sexual problems, weight loss or altered bowel habits. Her family history was not significant. She was 70 kg, 6-feets, 2 inches, breasts developed Tanner 3, no axillary hair and pubic hair Tanner 1, normal vaginal length, small cervix, huge mass, regular margins, firm and limited mobility with no visceromegaly, ascites or enlarged lymph nodes.

Pelvic ultrasound revealed large solid and cystic mass inseparable from small infantile uterus. On CT abdomen, there was 3.3 ×1.6 cm size uterus and a hypo-dense 16.9 x 12x 11 cm mass with solid and cystic areas, reaching up to the level of L-5 vertebra. There was loss of surrounding structures interface. The mass was displacing gut loops with no local and regional lymphadenopathy noted. Ca-125, Beta HCG, Alpha feto-protein, testosterone and LDH levels were within normal range. Alkaline phosphatase was 410 U/L, while LH/FSH levels were raised (35.4 IU/L, FSH 104.5 IU/L). Ultrasound guided trucut biopsy revealed dysgerminoma. Intra-operative findings showed 16 x 12 cm left adnexal mass, multiple solid and cystic areas, irregular margins and adherent left fallopian tube, small infantile uterus, right streak ovary and normal looking fallopian tube. Left salpingoophrectomy was done and histopathology report revealed a poorly differentiated neoplasm composed of nests and sheets of neoplastic cells, brisk mitotic activity with ovarian capsule, omentum and vascular invasion.

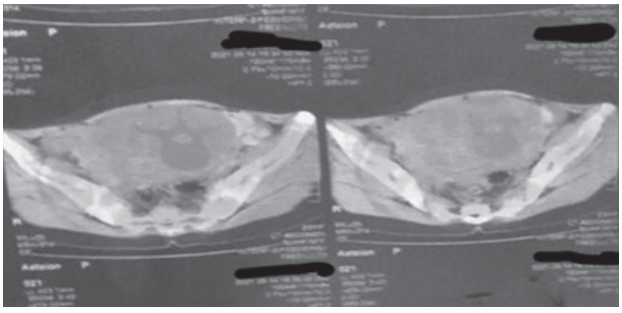

Fig 1: CT scan showing a huge hypo dense mass.

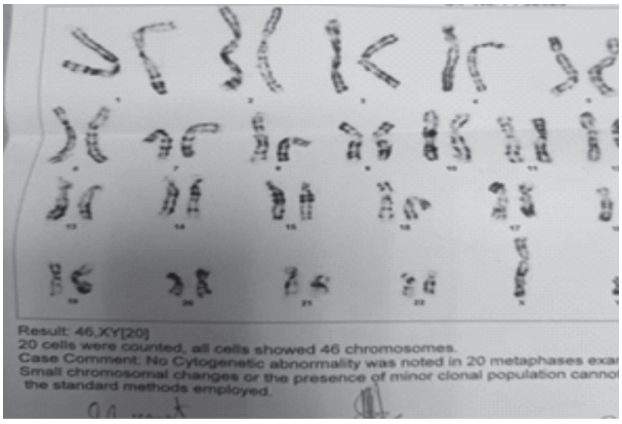

Fig 2: Karyotyping revealed a genotype of 46 XY.

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Fig 3: Left ovarian mass with adherent left fallopian tube.

DISCUSSION

Swyer syndrome is a very rare disorder of failure of sex organs development, first described in 1955 by Jim Swyer. [5] The incidence is 1 in 100,000. [2] Patients have XY chromosomal pattern, born as females, and present with a history of primary amenorrhea. [5,6] They have normal looking external genitalia, failure of development of secondary sexual characteristics, small infantile uterus, and streak gonads.

There may be molecular and genetic abnormalities (mutations) in different genes affecting SRY function, required for testicular formation. Some cases are not inherited and in some cases, exact cause remains unknown.[7] These patients have 46XY karyotype . The other differential diagnosis like Mayer–Rokitansky–Küster–Hauser syndrome, (XX) Turner syndrome, Congenital Androgenic Insensitivity Syndrome (XY) needs to be excluded.

These patients are at a high risk of developing germ cell tumors like gonadoblastomas and/or dysgerminomas due to presence of Y chromosome. The chance of Dysgerminoma to be malignant is high. [8,9] Treatment includes gonadectomy or pelvic clearance followed by chemotherapy in case of malignancy. Hormone replacement therapy may be considered for development of secondary sexual characteristics. These patients are infertile but may become pregnant by using donated eggs. Proper evaluation early diagnosis, counselling and psychological support is essential in the management of such patients. Prophylactic gonadectomy reduces the risk of developing germ cell tumor.

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xi) Departmental Permission Letter for the study.
xii) Letter of ethical review of concerned hospital/study place.
xiii) Bank draft for Rs. 5000/- (Rs. Five Thousand) in the name of Journal of Medical Sciences, Peshawar, Pakistan/or deposit in cash with Managing Editor Account No. 4048685170 (3548-9) Can be transferred ONLINE to the Account No. 4048685170 (3548-9) Branch Code 0388 at National Bank of Pakistan, University Campus Branch, Peshawar.

EDITORIAL POLICY

EDITORIAL POLICY OF JOURNAL OF MEDICAL SCIENCES (JMS), KHYBER MEDICAL COLLEGE, PESHAWAR

OVERVIEW

This document highlights the mission, objectives and editorial policy of JMS in regard to publication process by adhering to the guidelines by COPE (Committee in Publication Ethics) and ICMJE (International Committee of Medical Journals Editors). Each component of the editorial policy is explained in the next sections.

A MISSION OF JMS

To publish relevant, scientific and accessible material to help medical students and health professionals in their practice, teaching and learning, and career development

B OBJECTIVES OF JMS

a To publish clinical, epidemiological, public health, educational, translational, and allied sciences research to enable the scientists, clinicians and researchers to learn about developments and innovations in these disciplines

b To publish high quality descriptive and experimental research, review articles, editorials and case reports to enhance the understanding of scientific community regarding clinical practice and education

c To provide a platform for scientific community in promoting their career development through publishing quality research

C EDITORIAL POLICY

1 Open access

JJMS is an Open access scholarly literature source that is free of charge and often carries less restrictive copyright and licensing barriers than traditionally published works, for both the users and the authors. However, it complies with well-established peer review processes and tries to maintain high publishing standards.

2 Peer review process

The review process of JMS is following a "triage approach". Upon submission of a manuscript, either online or physical, the document undergoes a preliminary open (un-blinded) review in the office of the chief editor. The document is either accepted for further review, sent for revision back to the authors, or rejected at that time. Further review of JMS is following a blinded approach, where the article is sent to 2 reviewers, a local and international. During this process, all the relevant information about the authors and reviewers is kept confidential. However, we encourage to share reviewers' comments with co-reviewers of the same paper in a blinded manner, so reviewers can learn from each other in the review process. We also encourage the readers to send us the post publication reviews about a research work in the form of letters to the editors, which are then published and shared with the authors of relevant articles. The editorial board has the authority to retract an article if serious violation of credibility or quality of research is found after the article is published.

The journal is under no obligation to send submitted manuscripts for review, and under no obligation to follow reviewer recommendations, favourable or negative at all times. The editor of a journal is ultimately responsible for the selection of all its content, and editorial decisions may be taken by issues unrelated to the quality of a manuscript, such as suitability for the journal. An editor can reject any article at any time before publication, including after acceptance, if concerns arise about the integrity of the work.

3 Authorship

According to the ICMJE criteria, authorship is based on 4 criteria; (1) conceptualization and designing, (2) AND, data collection, (3) AND, writing and critical review, (4) AND, taking responsibility for the authenticity and integrity of all the research process. All those designated as authors should meet all these 4 criteria. The

co-authors should declare their roles and contributions in the research process explicitly. Those who do not meet all 4 criteria should be ACKNOWLEDGED only. If agreement cannot be reached about who qualifies for authorship, the institution(s) where the work was performed, not the journal editor, should be asked to investigate. If authors request removal, addition or change in the sequence of an author after manuscript submission or publication, journal editors should seek an explanation and signed statement of agreement for the requested change from all listed authors and from the author to be removed or added. The corresponding author is the one individual who takes primary responsibility for communication with the journal during the manuscript submission, peer review, and publication process. The corresponding author typically ensures that all the journal's administrative requirements, such as providing details of authorship, ethics committee approval, clinical trial registration documentation, and disclosures of relationships and activities, are properly completed and reported.

4 Submission of manuscript

The manuscript should be submitted through journal website which is using the Online Journal System (OJS) along with the Institution research and ethics board (IREB) certificate. The article should have the following format:

4.1: The abstract should be structured with word count of not more than 250 words.

4.2: The fonts should be Calibri, with size 12, and spacing of 1.5, with justified margins in MS office format.

4.3: The whole document should not be more than 3000 words (excluding references and appendices).

4.4: The number of figures and tables should not exceed 5 in the whole document.

4.5: The pictures and tables should be black and white in color.

4.6: Copied pictures and tables from other sources will not be entertained, unless a written approval from the original researcher and publisher is provided

5 Institutional research and Ethics board (IREB) certificate

Under no circumstances, an article will be accepted if approval from the relevant ethical board / committee is not taken before the start of a research. The board / committee should assess the proposal of a research in both ethical and technical aspects before giving a certificate of approval.

6 Conflict of interest

To ensure transparency in the research conduction, writing and publication, the authors, peer reviewers and editors have to declare conflicts of interest regarding financial aspects, academic competitions, and relationships during writing, reviewing and publishing the manuscripts. Details of sponsors along with their roles and access to data should be clearly stated.

7 Confidentiality

The editorial board in no way should publicize the work of a researcher in any form unless it is published. They should not publicize the comments and critique given by reviewers. Similarly, the reviewers are bound to keep the confidentiality of the work of researchers during and after the review. The work of researchers and the critique should never be discussed or exemplified in forums. The confidentiality of the researchers should be maintained in every possible way when the documents are sent for review. However, our review process is open (non-blinded) in the first phase, as per policy of the journal. In this case, the policy is clearly displayed on journal`s website for the researchers. Reviewers must not retain the manuscript for their personal use and should destroy paper copies of manuscripts and delete electronic copies after submitting their reviews. If a manuscript is rejected, it should be deleted from the editorial system. If an article is published, the manuscript along with its reviews and other relevant documents should be retained for a period of 3 years and then deleted. The only situation where confidentiality needs to be breached is when a situation of fraud or misconduct is found during the review process or after publication. Still, the authors and sometimes the reviewers, have to be notified.

8 Correction and retraction of articles

The guidelines for correction and retraction of articles are as follows:

8.1: A specific page is allocated in the journal (both electronic and printed) that will be used for news related to corrections in articles published in previous journals.

8.2: The editor should also post a new article version in the journal with details of the changes from the original version and the date(s) on which the changes were made.

8.3: Previous electronic versions will prominently note that there are more recent versions of the article (that will be placed at the end of abstract). Similarly, the more recent version should be cited by the authors or others.

8.4: If the error is judged to be unintentional, and the underlying science appears valid, and the changed version of the paper survives further review and editorial scrutiny, then retraction with republication of the changed paper, with an explanation, allows full correction of that research paper.

8.5: If serious violation of credibility or quality of a research paper is found after the publication, the article has to be retracted after approval of at least 3 members of the editorial board in consultation with chief editor. The whole process will follow the guidelines presented by Committee on publication ethics (COPE).

8.6: The retracted article should clearly be notified on the website and the word “retracted” should be mentioned along the title of the article.

9 Correspondence

Correspondence for submitting an article in JMS will be through a corresponding author. The duties of a corresponding author have already been presented in a previous section. Correspondence regarding debating an article is given high value and a separate page for letters to the editors has been allocated. Derogatory and demeaning letters are screened and letters which promote debates and critique are encouraged to be published. However, correspondence about the articles published in the last 1 year will be included only.

10 Fee submission process

The editorial board in a recent meeting has fixed a fee of 7000/- Rs (Pakistani), for local authors and 250 $ (US) for international authors. The fee should be submitted as bank draft/online payment through account (IBAN) no: PK56NBPA0388004048685170 (Branch code: 0388 / National Bank of Pakistan, University campus branch, Peshawar, Pakistan) as follows:

1) Article processing fee of 3000/- PKR at the time of submission of article after acceptance for preliminary / initial triage, open review by the Chief Editor. This amount will be non-refundable.

2) Article publication fee of 4000/- PKR at the time of acceptance of article after external review. This amount will be refundable if the article is rejected for any reason.

3) For international authors, the amount of 250 US dollars will be accepted after both internal and external review. Researchers belonging to countries other than Pakistan are advised to submit the fee after the whole process of review is completed and the article is accepted for publication.

11 Roles of editorial board, editors and members

The editorial board of JMS is following the Higher Education Commission (HEC) policy for research journals. The roles of the editorial board for JMS are mentioned below:

11.1: The roles of the Editorial Board are:

11.1.1: To offer expertise in their specialist area

11.1.2: To review submitted manuscripts

11.1.3: To advise on journal policy and scope

11.1.4: To work with the Editor to ensure ongoing development of the journal

11.1.5: To identify topics for special issues of the journal or recommend a Conference which would promote the journal, which they might also help to organize and/or guest edit

11.1.6: To attract new and established authors and articles

11.1.7: To submit some of their own work for consideration, ensuring that they adhere to Conflict of Interest rules and stating their relationship to the journal. This is very important as the journal cannot be seen to publish only papers from members of the Editorial Board.

11.1.8: It is important that Editorial Boards have a regular communication forum with other boards of similar nature, either face to face in person (depending on their country of origin, funding availability, etc.) or as more journals are doing today, communicating by teleconference, Skype or other web platforms.

11.2: The Patron:

The Patron is usually the Dean of the institute, and is overall incharge of the journal, who needs to be kept informed of the decisions taken by the editorial board. The patron is the final authority to approve the decisions and policies of the editorial board.

11.3: The Chief Editor:

11.3.1: The criteria for selection of Chief Editor are:

i. Expertise and experience in the specialist field related to the journal

ii. Publication record of a number of articles and /or books (usually in / related to the specialist field)

iii. Being a reviewer for an international peer reviewed journal

iv. Senior research position with equivalent experience in research and scholarship

v. Enthusiasm to undertake the Editor role

vi. Preferably a diploma, master or doctoral degree in Education and Research. It is not necessary to fulfill all the criteria to become a chief editor

11.3.2: The roles of Chief Editor are:

i. The key role of a journal`s chief editor is to promote scholarship in the specialist field associated with the journal, whilst also promoting the journal as the best journal to publish in. For any journal, the editor will need to encourage new and established authors to submit articles and set up a reliable panel of expert reviewers. Editors are also responsible for offering feedback to reviewers when required and ensure that any feedback to authors is constructive.

ii. An editor should also familiarize themselves with the Committee on Publication Ethics (COPE) 'Code of Conduct and Best Practice Guidelines for Journal Editors'.

iii. Depending on how the journal is managed and how it is structured, an Editor may have to make all the decisions regarding which articles to accept or reject for publication.

11.3.3: Managing editor:

The roles of manging editor are:

i. To help the chief editor to achieve the above-mentioned goals

ii. To communicate with the authors, reviewers, publishers and other agencies for smooth running of the journal

iii. To regularly evaluate the research work

iv. To communicate with funding and regulating agencies (HEC and others) for grants and accreditations.

11.3.4: Executive editor:

The roles of executive editor are:

i. To evaluate the research articles presented for publication

ii. To help the editorial board in policy making

iii. The help the editorial board in smooth publishing

iv. To communicate with reviewers and collaborate with external agencies for relevant purposes

11.3.5: Section editors:

Section editors are allotted different responsibilities. Some of these are mentioned below:

i. Bibliography

ii. Proof-reading

iii. Academic writing reviewing, grammar and spell checking

iv. Dissemination of articles for review

v. Contact with publishers under the supervision of senior editorial team

vi. Training of future reviewers, young members and other faculty members

vii. others

11.3.5: Editorial advisory board:

Editorial advisory board members consist of national and international senior academicians, researchers, clinicians and others to help the current editorial board in designing, implementing and evaluating policies regarding upgrading the quality of research work. These people also share best practices to help the editorial team to refine their research work.

12. POLICY REGARDING RECRUITMENT AND CONTINUATION OF EDITORIAL BOARD

Policy for recruitment and continuation of the editorial board is based on the guidelines discussed in the previous section. The chief editor, managing editor and executive editors are recruited by the patron in-Chief. Members are then selected by them from amongst the faculty who have an aptitude for research, and their names are endorsed by the patron. The tenure of editorial board is decided by the Patron after a period of 3 years whether to continue or recruit a new team or member. The editorial advisory board members are recruited for indefinite period by the editorial team of JMS.

13. Plagiarism policy

he journal is following the plagiarism policy of Higher Education Commission of Pakistan, and for this purpose, a plagiarism standing and review committee has been established under the chairmanship of Chief Editor of JMS along with 4 members amongst senior faculty. The committee has been given the authority to review research papers and plagiarism complaints related to published work in the journal.

14 Contact information

The office of managing editor or chief editor should be contacted anytime in working hours or can be contacted through their emails for correspondence.

REFERENCES

1. ICMJE recommendations
2. COPE guidelines
3. SCOPUS

This document is prepared in January 2020 to be used by editorial board, reviewers, researchers and faculty as a guide to make them aware of policies and procedures of publishing, conducting, writing, reviewing and evaluating the research published in JMS. This document is developed by including the recommendations of ICMJE (2019) and COPE guideline and in case of any conflict, lack of clarity and ambiguity, the recommendations of latest ICMJE recommendation and COPE will prevail.

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Key to abbreviations

OA = Original Article

ED = Editorial

KHYBER MEDICAL COLLEGE, PESHAWAR - PAKISTAN