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Diabetes Mellitus – The Epidemic of 21st Century

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Diabetes is one of the commonly experienced diseases worldwide but it is more commonly seen in third world countries like Pakistan, India, Bangladesh, and others. It is considered as the epidemic of the 21st century. According to International Diabetes Federation (IDF) 2021 figures, 537 million adults (20-79 years) are living with diabetes all over the world (1 in 10 people) and this is predicted to be 634 million by 2030. Over 3 in 4 adults with diabetes live in low- and middle-income countries. Pakistan is one of the most affected countries in the world and is ranked 3rd by the number of adults with diabetes after China and India. Approximately, 33 million adults are affected with diabetes in Pakistan and overall prevalence is about 26.7%.[1]

Diabetes mellitus is a metabolic disease that results from insulin deficiency and or peripheral insulin resistance. It can affect people of all age groups. There are several types of diabetes but Type 2 Diabetes Mellitus (T2DM) is the most common with 90% of all the diabetics being affected with this type. This type usually affects the adults and becoming more common in obese people. Long-term diabetes may proceed to serious, chronic complications having impact on the lives of individuals, families and societies. Patients are usually asymptomatic or have less or vague symptoms, diagnosed late and may be already having serious complications. It may affect the major organs of the body and may lead to blindness, renal failure, stroke, cardiovascular disease and diabetic foot complications. It is also considered as one of the major causes of cardiac related deaths being two third of the diabetic patients die of cardiovascular disease.

In an adult, genetic factors and life style changes are the main predisposing factors to develop diabetes. Life style factors include obesity, a sedentary lifestyle, and the intake of more processed food with higher sugar content. In Pakistan, obesity is becoming more prevalent and in one of the study the overall prevalence of generalized obesity was 57.9% (42% in males and 58% in females), and central obesity was 73.1% (37.3% in males and 62.7% in females) in Pakistan.[2] Our children and young adults are developing a habit of using canned and highly processed food more frequently along with little to no physical activity hence leading to surge in obesity. These bad dietary habits and early development of obesity predispose our children and young adults to develop pre-diabetes thus increasing the risk of changing to diabetes in the coming years. The increased urbanization coupled with the adaptation to the urban sedentary life style makes the possible increase in the number of cases even more concerning. Many Pakistanis live in rural areas and a lack of access to affordable education also plays a role in growing diabetes cases. Many people even in urban areas don't understand that diabetes is a silent killer and many seek medical advice when their health status already declined due to diabetic complications.[3]

Management of diabetes revolves around healthy balanced diet, physical activity and pharmacological measures. Eating more of vegetables and fibrous foods avoiding sugary products make it a well-balanced healthy diet. Optimization of the body weight with daily physical activity in the form of 150 minutes' brisk walk per week is mandatory for the better management of diabetes. Great advances are made in the pharmacological management of diabetes with new drugs coming up not only having good control of diabetes but also providing cardiovascular safety and protection. SGLT2-i (Sodium-glucose co-transporter-2 Inhibitors) and GLP1-RA (Glucagon-like peptide-1 receptor agonists) are new drugs commonly used for the better control of diabetes and reducing the risk of complications. Most of these new treatment modalities are costly. The high cost along with poor compliance to the medication adds together with more number of diabetic patients with complications.

There are several diabetes myths that prevail within Pakistan due to which healthcare professionals and

patients suffer from improper treatment plans leading to harmful consequences in diabetic patients.[4] People believe that increased consumption of sugar leads to diabetes, but actually consumption of sugary products does not have any direct link to diabetes but it does have an association with lifestyle changes, development of obesity and pre-diabetes. They are prone to develop diabetes at early age. As diabetes is one of the major health hazards leading to long-term complications and concerns for most patients, one should avoid incorrect information about diabetes. Most of the people in our society are unaware of the impact of lifestyle modifications on our health in terms of prevention, control, and treatment for diabetes and most people are not even aware of the normal range of blood sugar levels. It is therefore essential to provide correct information about lifestyle changes when offering diabetic treatments. The best and economical diabetic treatments should be provided to the people and attention should be paid to the health status and lifestyle of the patients.

In our country many people don't take diabetes seriously and at times heard saying that their sugar is little high or just have a touch of diabetes. They should be educated that diabetes is a serious disease and they must learn to manage it. They must not let the diabetes to affect their body with physical complications of diabetes and even have an impact on quality of life. They need to make healthy food choices, stay at a healthy weight, move more every day, and take their medicine even when they feel good. Although it's not easy, but it's worth to adopt such behavior and compliance.[5]

The medical experts also believe that bad dietary habits, lack of exercise and rising obesity are contributing to Pakistan's diabetes surge. This problem is attributed to the lack of sporting facilities, as well as limited public spaces for exercise, particularly in schools. Public hospitals are providing services to the diabetic patients and quite a few diabetic centers are established but these setups are insufficient for provisions of good diabetic care to many people. Rising health care costs and poverty also play important role in poor management of diabetes. In last few years the prices of the medication have skyrocketed, steering away many patients.[6] The government cannot solve the country's health problem alone, especially this very high number of diabetics in our society, unless people change their lifestyle and dietary habits. The problem will continue to haunt us and millions of more people will suffer from it in the coming years. It is not solely the responsibility of health care professionals but other strata of society like religious and social media influencers should step forward to combat this growing challenge. More awareness of the disease needs to be raised nationwide through social, news and print media and even by starting health education at school level.

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Ligasure Vessel Sealing Versus Conventional Suture Ligation in Thyroidectomy

Ahmad Rafique,[1] Fawad Hameed,[2] Muhammad Khurram Jameel,[3] Humaira Alam,[4] Hafiza Shehla Arshad,[5] Ahmed Kaleem,[6] Maham Qazi[7]

Abstract

Objective: To evaluate the efficacy of ligature sealing versus standard suture sealing for multinodular goiter patients after thyroidectomy.

Method: The aim of our study is to evaluate the efficacy of ligature sealing versus standard suture sealing for multinodular goiter patients after thyroidectomy. The research was done in the Mayo Hospital in Lahore, Pakistan, specifically in the General Surgery Division. Ligasure-sealed patients made up Group A, while those in Group B were treated with traditional suture-ligation. The average duration of surgery, the average amount of discomfort felt by the patient afterward, and the average amount of drain fluid collected after surgery were all recorded.

Results: Eighty people in total participated in the study. Patients in Group-A had an average operation time of 67.3±6.9 minutes, while those in Group-B averaged 85.6±8.3 minutes; this difference was statistically significant (p0.000001). Patients in group A reported an average of 2.6±1.3 units of pain, while those in group B reported 1.7±0.7 units of pain; this difference was statistically significant (p 0.001). Patients in Group-A had a mean drain output of 53.5±4.9 ml following surgery, while those in Group-B had an output of 68.2±7.3 ml; this difference was statistically significant (p = 0.0001).

Conclusion: Thyroid surgery using ligature sealing is an effective and safe alternative to the standard approach, resulting in significantly less downtime, less discomfort, and less drainage after the procedure.

Keywords: Ligasure Sealing, Conventional Technique, Multinodular Goiter, Thyroidectomy.

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Introduction

Ligasure is an electro thermal bipolar tissue sealing device used in many surgeries, and numerous diathermy approaches have been used to decrease intra-operative blood loss.[1-3] The Ligasure is an automatic feedback-controlled response system with high-current, low-voltage bipolar radiofrequency which automatically interrupts power in accordance with the composition and impedance of the tissue between the instrument's jaws.[4]

Although total thyroidectomy is the surgical treatment for benign and malignant thyroidal diseases, problems might arise from overly aggressive excision.[5] Bleeding during thyroidectomy can make it difficult to safely separate the recurrent laryngeal nerve and parathyroid gland. Thyroid surgery requires careful devascularization of the gland, as the thyroid has one of the greatest blood supply of any organ due to the large number of blood arteries and plexuses that penetrate its parenchyma. Therefore, it is crucial to achieve hemostasis prior to gland excision by separating the different arteries.[6]

Newer methods of vessel haemostasis, such as ligasure, offer an alternative to the more invasive bipolar surgical

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diathermy system and can achieve the same hemostasis results as the suture knot tying procedure.[7] Due to the considerable resection undertaken, postoperative bleeding problems and hematoma formation are slightly more common after complete than partial thyroidectomy.[8]

Thyroid surgery requires careful hemostasis due to the abundant blood flow provided by the gland's many blood arteries. Hemostasis is typically achieved during dissection by ligating both ends of the vessels; a process traditionally accomplished using hand-tied ligatures or sutures. Hemostasis can be achieved with the use of several cutting devices (bipolar electrocautery, lasers, clips, and staples) that have been developed over the past few decades.[12]

The purpose of this study is to evaluate the efficacy of ligature sealing versus standard suture sealing for multinodular goiter patients after thyroidectomy.

Material and Methods

The research was done in the Mayo Hospital in Lahore, Pakistan, specifically in the General Surgery Division. Between June 10th and November 10th, 2019, the research was conducted. A cross-sectional design was used for this study. Simple comparative analysis was employed for this research.

With an expected mean operative time of 127.1± 20.95 minutes using conventional suture- ligation and 115.54± 15.35 minutes using ligasure sealing in patients with multinodular goiter undergoing thyroidectomy, a sample size of 80(40 in each group) is estimated using 95% confidence interval and 80% power of test.[9]

Patients of both sexes, aged 18-60 years, undergoing thyroidectomy for MNG (as per operational definition), were included; however, those with Graves' disease (also known as diffuse toxic goiter, an autoimmune disease characterised by hyperthyroidism due to circulating auto antibodies against TSH receptors) or toxic MNG (a multinodular goiter with clinical symptoms (heat tolerance, weight loss, palpitations) and signs (T4 and TSH receptor antibodies), Neck irradiation history, malignancy in the MNG confirmed prior to surgery, Presence of metastases (as determined by a physical exam), evidence of recurrence of cancer (as documented in the medical record), and an insufficient FNAC sample prior to surgery.

Eighty patients were enrolled from the Surgical Wards of the Department of Surgery at Mayo Hospital in Lahore after receiving approval from the hospital's ethics council. There were 80 patients total, and they were split evenly between Group A (40 people) and Group B (20 people). Ligasure sealing was used on patients in Group A, while traditional suture ligation was used on patients in Group B.

Patients gave their consent after being fully informed about the trial. Each patient's name, age, and gender were recorded. After the patient was admitted to the hospital, a full history and physical examinations were performed to arrive at the preliminary diagnosis. Blood tests and ultrasound of the neck were used to determine the prevalence of nodules and calcification in each patient. Then patients underwent thyroidectomy with predictable safety of recurrent laryngeal nerve and parathyroid gland.

The same general surgical team performed all of the surgeries, which were all done while the patient was under general anaesthesia. Patients were moved to the ward when surgery was completed. Metrics such as drain output, surgical time, and postoperative discomfort were recorded. A pre-made Performa was used to collect all of the information.

SPSS v25.0 was used to enter and process all data. Mean with S.D. was used to characterize the ages of the subjects, the duration of the procedures itself, the volume of drainage from the surgical incision, and the severity of the pain experienced after surgery. Frequencies and percentages were used to characterize the gender distribution. To account for potential effect modifiers, data were stratified by age, body mass index, and gender. Groups were compared using a t-test after they were stratified. We regarded a p-value less than <0.05 to be statistically significant.

Results

Total 80 patients enrolled in this study were divided in two groups i.e. Group-A (Ligasure Sealing) and Group-B (Conventional Technique). Group-A had 19(47.5%) males and 21(52.5%) females. In group-B, 16(40.0%) were males and 24(60.0%) females. In group-A, there were 3(7.5%) in 18-30 years age group, while 22(55.0%) and 15(37.5%) were in 31-45 years and 45-60 years age groups respectively. In group-B, there were 9(22.5%) in 18-30 years age group, while 16(40.0%) and 15(37.5%) were in 31-45 years and 45-60 years age groups respectively. In group-A, there were 28(70.0%) who had normal BMI, while 10(25.0%) and 2(5.0%) were overweight and obese respectively. In group-B, there were 25(62.5%)

Table 1: *Comparison of variables according to the number of patients.*

		Groups		Total
	Gender	Ligasure Sealing	Conventional Technique	
Comparison of gender distribution between groups	Male	19	16	35
		47.5%	40.0%	43.8%
	Female	21	24	45
		52.5%	60.0%	56.3%
	Total	40	40	80
		100.0%	100.0%	100.0%
	Age groups	Group		Total
		Ligasure Sealing	Conventional Technique	
Comparison of age groups between groups	18-30 years	3	9	12
		7.5%	22.5%	15.0%
	31-45 years	22	16	38
		55.0%	40.0%	47.5%
	45-60 years	15	15	30
		37.5%	37.5%	37.5%
	Total	40	40	80
		100.0%	100.0%	100.0%
	BMI	Groups		Total
		Ligasure Sealing	Conventional Technique	
Comparison of BMI between groups	Normal (18-24.9)	28	25	53
		70.0%	62.5%	66.3%
	Overweight (25-29.9)	10	12	22
		25.0%	30.0%	27.5%
	Obese (>30)	2	3	5
		5.0%	7.5%	6.3%
	Total	40	40	80
		100.0%	100.0%	100.0%

who had normal BMI, while 12(30.0%) and 3(7.5%) were overweight and obese respectively. The mean operative time of patients in group-A was 67.3±6.9 minutes and in group-B was 85.6±8.3 minutes with p-value of 0.000001 which is statistically significant. The mean pain score of patients in group-A was 2.6±1.3 and in group-B was 1.7±0.7 with p- value of 0.001 which is statistically significant. The mean post-operative drainage of patients in group-A was 53.5±4.9 ml and in group-B was 68.2±7.3 ml with p-value of 0.000001 which is statistically significant.

Discussion

With one notable exception being the technique for performing a thyroidectomy, which saw no advancements other than the adoption of monopolar electrocautery for dissection due to several routine, practical, and technical issues. Staplers, which are not only prohibitively expensive, are also too limited in their applications to be useful during thyroid surgery. Both lasers and bipolar electrocautery pose risks to nearby essential organs, vessels and nerves e.g recurrent laryngeal nerves, parathyroid glands.[13]

Ultrasonically activated shear introduced in 1990s is an alternative way of achieving hemostasis. This apparatus works on the principle that ultrasonic energy can be transformed into mechanical motion.[14] A novel Hemostatic system is the Sealing Precise Diathermy Technology used in both open and endoscopic surgical procedures, with a decrease in the operating time and fewer intraoperative complication faced in the OR due to bleeding. A number of surgical procedures, including those involving the abdomen, the chest and many others, have been found to benefit from shorter operating times.[17-18]

We compared a total of 80 patients, 40 patients who underwent total thyroidectomy using Ligasure Sealing, 40 patients who underwent total thyroidectomy using conventional method. Ashkenazi et al.[19] reported sutureless thyroidectomy using LS, and reported the main advantage of using Ligasure device for achieving hemostatic is the reduced operation time duration and the reduction of risks associated with using sutures and clips. Another study by Sandonato et al.[20] documented that 67 patients underwent total thyroidectomy with the help of LS, and noted that complications, such as transient recurrent nerve palsy and hypo-parathyroidism,

Table 2: *Operative time, Pain Score and Drainage Comparison between Two Groups*

Comparison of operative time between groups	Operativetime (minutes)	Groups	n	Mean	Std. Deviation	p-value
		Ligasure Sealing	40	67.3	6.9	0.000001
		ConventionalTechnique	40	85.6	8.3	
Comparison of pain score between groups	Pain score	Ligasure Sealing	40	2.6	1.3	0.001
		Conventional Technique	40	1.7	0.74	
Comparison of drainage between groups	Drainage (ml)	Ligasure Sealing	40	53.5	4.9	
		Conventional Technique	40	68.2	7.3	0.000001

Table 3: *Overall the Results are showing the Percentage of each Variable with Significant the P-value between Two Groups.*

Stratification of operative time between groups with respect to gender	Operativetime (minutes)	Gender	Groups	n	Mean	Std. Deviation	p-value
		Male	Ligasure Sealing	19	66.5	6.5	
			Conventional Technique	16	85.1	8.4	0.000001
		Female	LigasureSealing	21	68.1	7.3	0.000001
			Conventional Technique	24	85.9	8.4	
Stratification of pain score between groups with respect to gender	**Pain score**	Male	Ligasure Sealing	19	2.6	1.3	0.020
			Conventional Technique	16	1.7	0.6	
		Female	Ligasure Sealing	21	2.5	1.5	0.024
			Conventional Technique	24	1.8	0.7	
Stratification of drainage between groups with respect to gender	**Drainage (ml)**	Male	Ligasure Sealing	19	54.1	4.7	0.000001
			Conventional Technique	16	68.3	7.1	
		Female	Ligasure Sealing	21	52.9	5.1	0.000001
			Conventional Technique	24	68.1	7.6	
Stratification of operative time between groups with respect to age	**Operativetime (minutes)**	18-30 years	Ligasure Sealing	3	68.1	8.1	0.014
			Conventional Technique	9	85.8	9.2	
		31-45 years	Ligasure Sealing	22	66.8	6.7	0.00001
			Conventional Technique	16	84.3	7.9	
		45-60 years	Ligasure Sealing	15	67.9	7.4	0.0001
			Conventional Technique	15	86.8	8.6	
Stratification of pain score between groups with respect to age	**Painscore**	18-30 years	Ligasure Sealing	3	2.3	1.5	0.429
			Conventional Technique	9	1.7	0.8	
		31-45 years	Ligasure Sealing	22	2.5	1.3	0.023
			Conventional technique	16	1.6	0.7	
		45-60 years	Ligasure Sealing	15	2.8	1.5	0.042
			Conventional Technique	15	1.8	0.7	
Stratification of drainage between groups with respect to age	**Drainage (ml)**	18-30 years	LigasureSealing	3	57.3	2.8	0.025
			ConventionalTechnique	9	70.1	7.9	
		31-45 years	LigasureSealing	22	53.4	4.9	0.0001
			Conventional Technique	16	67.7	7.7	
		45-60 Years	Ligasure Sealing	15	52.8	5.1	0.0001
			Conventional Technique	15	67.6	6.9	
Stratification of operative time between groups with respect to BMI	**Operative time**	Normal (18-24.9)	Ligasure Sealing	28	67.1	6.7	0.0001
			Conventional Technique	25	84.1	8.7	
		Overweight (25-29.9)	Ligasure Sealing	10	68.8	7.2	0.00001
			Conventional Technique	12	87.8	7.3	
		Obese (>30)	Ligasure Sealing	2	63.1	9.8	0.0001
			Conventional Technique	3	89.6	7.7	
Stratification of pain score between groups with respect to BMI	**Painscore**	Normal (18-24.9)	Ligasure Sealing	28	2.5	1.4	0.008
			Conventional Technique	25	1.6	0.7	
		Overweight (25-29.9)	Ligasure Sealing	10	2.8	1.3	0.101
			Conventional Technique	12	2.1	.7	
		Obese (>30)	Ligasure Sealing	2	2.1	.7	0.219
			Conventional Technique	3	1.3	0.5	
Stratification of drainage between groups with respect to BMI	**Drainage (ml)**	Normal (18-24.9)	Ligasure Sealing	28	53.4	5.4	0.0001
			Conventional Technique	25	69.2	7.8	
		Overweight (25-29.9)	LigasureSealing	10	52.9	3.6	0.00001
			Conventional Technique	12	66.8	6.1	
		Obese (>30)	LigasureSealing	2	57.1	2.8	0.285
			Conventional Technique	3	65.3	8.3	

were significantly less frequent than they had reported in another analysis of 579 total thyroidectomy cases.[21]

Operation time, pain rating, and volume of postoperative drain output were all significantly different between the Ligasure Sealing and conventional methods in our study. Operating time for Patients in the ligature sealing group was 67.3±6.9 minutes, while those in the conventional group underwent surgery for a mean of 85.6±8.3 minutes. Patients in the ligature sealing group reported a mean pain score of 2.6±1.3, while those in the traditional group reported a score of 1.7±0.7. Patients in the ligasure sealing group had a mean drainage of 53.5±4.9 ml, while those in the traditional group had a mean drainage of 68.2±7.3 ml.

Conclusion

Ligasure sealing is a safe alternative to conventional technique in thyroid surgery, allowing for a significant reduction of operative time, pain score and post-operative drainage.

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Conflict of Interest: *None*

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Authors Contribution

AR: Conceptualization of Project
FH, HA: Data Collection
AR: Literature Search
MKJ: Statistical Analysis
HSA, AK: Drafting, Revision
HSA: Writing of Manuscript

Comparative Evaluation of High Versus Low Pressure Pneumoperitoneum in Causing Acute Kidney Injury During Laparoscopic Cholecystectomy

Junaid Khan Lodhi,[1] Asim Malik,[2] Saba Tahir Bukhari,[3] Saima Amjad,[4] Tasadduq Hussain,[5] Ossama Ather[6]

Abstract

Objective: Aim of our study is to monitor low- and high-pressure pneumoperitoneum effects and find optimum intra-abdominal pressure that is safe to avoid or minimise acute kidney injury.

Method: This study was conducted at Fatima Memorial hospital from July 2022 to December 2022. A total of 80 patients were segregated into two groups of 40 each. Group A had laparoscopic cholecystectomy with 15 mmHg pneumoperitoneum pressure while Group B had 20 mmHg pneumoperitoneum pressure. Patients were monitored postoperatively for creatinine and urine output changes at 8 hours, 24 hours and 72 hours interval.

Results: Post-operative creatinine rise and fall in urine output was statistically significant between both groups, indicating 15 mmHg pneumoperitoneum is safer for laparoscopic cholecystectomy to avoid acute kidney injury (AKI). Operation time, inflation time and blood loss were statistically significant and remain the key factors in predicting AKI after laparoscopic cholecystectomy.

Conclusion: AKI is a transient condition that can arise after laparoscopic cholecystectomy. It can be minimized by keeping intra-abdominal pressure ⩽ 15mmHg. Operation time, inflation time and perioperative blood loss can predict AKI per-operatively.

Keywords: Laparoscopic cholecystectomy, Pneumoperitoneum, Acute kidney injury

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Introduction

Gall stone disease is a chronic hepatobiliary disease impacting negatively on world economy.[1] Laparoscopic cholecystectomy has now been accepted as standard treatment worldwide for cholelithiasis.[2] Since the advent of laparoscopy, abdominal surgery has been revolutionized. Its merits include smaller incision size, lesser pain postoperatively, early ambulation with faster recovery and return to routine activities and work.[3,4] For successful and effective laparoscopy, creation of pneumoperitoneum is first and pivotal step as better perception and movement of laparoscopic instruments peroperatively is not possible without it. The commonly used gas to insufflate peritoneal cavity is carbon dioxide (CO_2). Certain physiological alterations have been reported while creating pneumoperitoneum, especially the renal functions.[4] Many authors have shown conflicting reports while trying to establish relationship between CO_2 induced pneumoperitoneum and renal functional changes in animal models. Chiu and colleagues used well hydrated pigs and reported a 60% reduction in blood flow to kidney after 2 hours of CO_2 insufflation which returned to normal after desufflation.[5] Kirsch and associates showed in pigs that at a pressure of 15mmHg of pneumoperitoneum, Inferior vena cava (IVC) blood flow decreases and resultantly decreasing urine output and increasing serum creatinine.[6] On the contrary, Ali and Yavuz with associates showed that renal perfusion is preserved even after a pneumoperitoneum greater

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than 15mmHg.[7,8] According to Kidney Disease Improving Global Outcomes (KIDGO) criteria, AKI is defined as increase in serum creatinine ≥ 0.3mg/dl within 48 hours or urine volume < 0.5ml/kg/hour for 6 hours.[9] Data in this context is Pakistan is almost nil. No human study is available in Pakistani set up to validate these findings for laparoscopic cholecystectomy.

Material and Methods

After approval from IRB letter no. FMH-11/10/2022-IRB-1113 dated December 01,2022, this single centred quasi-experimental study was conducted at Surgical floor, Fatima Memorial hospital, Lahore between July 2022 to December 2022. Sample size was 80. All patients above 18 years of age, with ASA status between I to III, having symptomatic gall stones were included in the study. Patients with pre-existing chronic kidney disease and those on NSAID therapy were excluded from the study as they could affect post-operative renal physiology. After taking informed consent, all patients underwent laparoscopic cholecystectomy. Same anaesthetic agent with standard dose was used in all patients. Those patients who were suspected to have simple cholecystectomy were subjected to 15mmHg pressure of pneumoperitoneum and labelled as group A, while those with difficult cholecystectomy were subjected to 20mmHg pressure of pneumoperitoneum labelled as group B. Standard treatment was offered to all the patients post-operatively including IV fluids, IV antibiotics and analgesia. Blood samples were taken for serum creatinine estimation before surgery, 8 hours, 24 hours and 72 hours after surgery. Urine output was measured 8 hours, 24 hours and 72 hours after surgery. Similarly, operation time, insufflation time and blood loss were also calculated. All the data was recorded in structured proforma. AKI was assessed by following KIDGO criteria. Statistical analysis was performed on SPSS version 21. Descriptive statistics were computed and described as mean ± SD. Categorical variables were stated using frequency distribution. Paired samples were subjected to t test. P value of less than 0.05 was taken as significant.

Results

A total of 80 patients were included in the study and divided into two groups of 40 patients each. Group A patients had 15mmH pressure while group B had 20mmHg pressure of pneumoperitoneum. The demographic characteristics of the two groups and its statistical significance is summarised in table 1. No statistical difference was found between two groups. The serum creatinine and urine output both started to be affected 8 hours after surgery. The serum creatinine reached its peak 24 hours after surgery. However, it started to decline and return to normal after 72 hours. Similarly, urine output declined to a minimum 24 hours after surgery but returned to normal after 72 hours of surgery. These results are shown in) Fig-1 & 2). Certain intraoperative parameters were calculated and measured and then compared in both groups to predict AKI postoperatively. Our results are summarised in (Table-2). The number of patients having AKI and non-AKI in both groups is summarised in (Table-3). These results make it clear that a pressure of 15mmHg is an optimum pressure to maintain pneumoperitoneum while minimising acute kidney injury during laparoscopic cholecystectomy.

Table 1: *Demographic Data & Statistical Significance*

Variable	Group A	Group B	P value
Age (in years)	41.92± 8.62	42.70± 8.07	0.681
Gender (M: F)	8: 32	12: 28	0.439
BMI (Kg/m²)	25.5± 3.88	26.1± 2.95	0.729
Preoperative creatinine level(mg/dL)	0.83± 0.24	0.88± 0.18	0.274

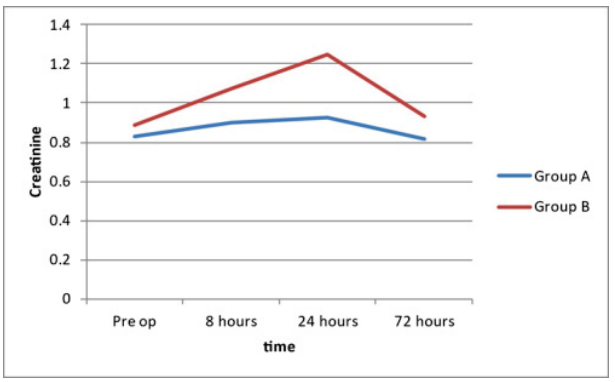

Fig-1. *Postoperative creatinine levels comparison at different time intervals.*

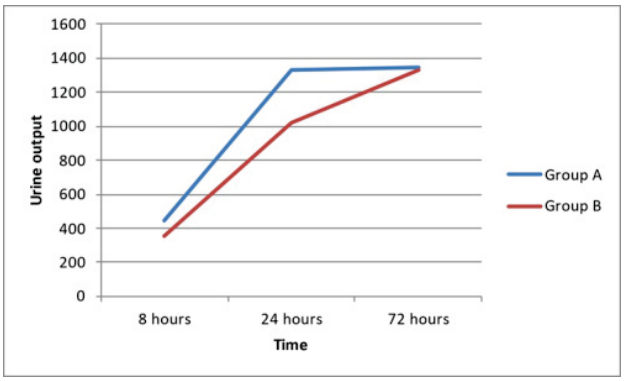

Fig-2. *Postoperative urine output comparison at different time intervals.*

Table 2: *Role of clinical intraoperative parameters in predicting AKI*

variable	Group A	Group B	P value
Creatinine level 8 hours after surgery (mg/dL)	0.89± 0.23	1.07±0.28	0.003
Creatinine level 24 hours after surgery (mg/dL)	0.92± 0.31	1.24±0.49	0.001
Creatinine level 72 hours after surgery (mg/dL)	0.81± 0.19	0.93±0.16	0.005
Urine output 8 hours after surgery (ml)	444± 83.26	357.75± 130.23	0.001
Urine output 24 hours after surgery (ml)	1333.25± 256.65	1017.25± 379	0.0001
Urine output 72 hours after surgery (ml)	1347.50± 160.50	1332.5± 153.81	0.671
Operation time (minutes)	119.05± 11.73	126.95± 14.39	0.009
Insufflation time (minutes)	92.50± 18.16	109.65±17 .40	0.0001
Blood loss (ml)	98± 34.5	137.75± 39.6	0.0001
Length of stay (days)	4.05± 4.9	4.08± 1.8	0.976

Table 3: *Crosstabulation of patients having AKI &non-AKI in both groups.*

AKI	Group A	Group B	Total
Yes	4 (10%)	15 (37.5%)	19 (23.9%)
No	36 (90%)	25 (62.5%)	61 (76.1%)
Total	40 (100%)	40 (100%)	80 (100%)

Discussion

This study demonstrated the fact that AKI is a fairly common condition that can occur during laparoscopic cholecystectomy. Incidence of AKI in our study is 19 (23.9%) in total which is in contrast to other studies as shown by Boyer et al. and Abdullah et al. that found incidence of AKI of 2.3-2.9% following bariatric surgery.[10,11] The limitation of these studies is that urine output was not included in diagnostic criteria. We followed KIDGO guidelines using both serum creatinine and urine output as an AKI detection criterion. However, Srisawat et al. concurred with our findings by using KIDGO guidelines and reported AKI incidence of 35.9%.[12] Our study proposed that operation time and insufflation time both is strongly associated with AKI with group B patients affected more for having an intra-abdominal pressure of 20mmHg. This fact is supported by Brusasco et al. who showed decreased renal function in pigs with an intra-abdominal pressure of ≥20mmHg.[13] Similarly, operation time was associated with AKI after laparoscopic cholecystectomy which is also concurred by some authors that an operation time of >210 minutes enhanced AKI risk from 0.8-4.4%.[4,14] We strongly suggest not only to keep intra-abdominal pressure at ≤ 15mmHg but also limit operation time and insufflation time to avoid risk pf perioperative acute kidney injury.

Increased intra-abdominal pressure cause renal function disturbance by three proposed mechanisms. First is chemical mechanism caused by hypercarbia due to CO_2 inflation. Second is mechanical effect due to increased intra-abdominal pressure compressing renal veins and impeding blood flow to kidney.[13] Third mechanism is hormonal involving renin-angiotensin-aldosterone system. It denotes renal vasoconstriction thereby increasing renin, aldosterone and antidiuretic hormone during laparoscopic gastric bypass surgery.[15] It is important to clarify that all the patients in our study had transient AKI, resolving spontaneously after 72 hours with nil mortality. This finding is in contrast to other researchers who have reported a higher mortality by 1.07-2.01 times.[16,17] We owe this difference to better ICU facilities with dedicated doctors and paramedical staff, an aggressive management of AKI since the start and better selection of patients. Blood loss was also noted to be a statistically significant factor in our study in predicting AKI. It occurred during dissection within calots triangle. Our findings are in accordance with the studies done earlier in this regard.[18]

Conclusion

AKI is a transient condition that can arise after laparoscopic cholecystectomy. It can be minimized by keeping intra-abdominal pressure ≤ 15mmHg. Operation time and inflation time can predict AKI perioperatively. Further studies with large randomized controlled trial using novel biomarkers for kidney injury is required to validate this notion.

Conflict of interest *None*

Funding Source *None*

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Authors Contribution

AM: Conceptualization of Project
TH: Data Collection
STB: Literature Search
OA: Statistical Analysis
SA: Drafting, Revision
JKL: Writing of Manuscript

Minimally Invasive Percutaneous Plate Osteosynthesis (MIPO) for Distal Tibial Metaphyseal Fracture: A Better Option

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Abstract

Objective: The objective of this study was to evaluate the radiological and functional outcomes for treatment of fracture distal tibial metaphysis fixed with pre-contoured anatomical locking compression plate using minimally invasive percutaneous plate osteosynthesis (MIPO) technique.

Method: This was a prospective study conducted at Department of Orthopedic Surgery, Services Hospital, Lahore. Total of 58 closed distal tibial metaphyseal fractures (AO classification 43A) included in the study. All patients were operated using anatomical LCP with MIPO technique. The functional outcome was assessed by Tenny & Wiss criteria at 6 weeks intervals with final scoring at 24th week. Functional outcome was graded as excellent, good, fair and poor. Similarly, radiological outcome was also assessed at 6 weeks intervals using Hammer et al criteria and grade 3 labelled as union.

Results: We observed excellent functional outcome in 48 patients (82.6%) and good outcome in 6(10.34%) at last follow-up. Radiological union was achieved in 100% (58) patients at 24th week. The average time of union was 16.5 weeks with a range of 12 to 23 weeks. Three patients (5.17%) developed superficial wound infection which was successfully managed with antibiotic therapy and no surgical site deep infection reported.

Conclusion: Results of this study advocate that treatment of distal tibial metaphyseal fractures with LCP by MIPO technique is an effective modality resulting in less complication, high bone union and good functional outcome.

Keywords: Locking compression plate, minimally invasive percutaneous plate osteosynthesis

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Introduction

Tibial fractures occur due to high and low energy trauma. It has annual incidence of 17 per 100,000 population.[1] Treating distal tibial metaphyseal fracture is a difficult conundrum even for the experts. Various factors which guide the surgical plan includes pattern of fracture, extent of soft tissue involvement and quality of bone.[2,3] Four commonly used methods include casting or bracing, external fixation, internal fixation with plates and intra-medullary fixation. Conservative management with POP casting is associated with complications of ankle stiffness, loss of reduction, mal-union and non-union. External fixation is challenging and is associated at time with inaccurate reduction, spanning of the ankle joint, stiffness, and infection at pin tracts. Intramedullary nailing is troubled with less stability because of short distal segment.[4,5] Soft tissue viability and periosteal injury in distal fracture fixation poses complication risk with conventional methods of internal fixation using open technique. Secondarily the loss of precious fracture hematoma by soft tissue dissection done to attain anatomical reduction and periosteum stripping can cause

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delayed union or even non-union. To avoid these complications and the soft tissue devitalization.[6] Mminimally invasive plate osteosynthesis techniques has evolved. This method preserve the help-ful biological environment to promote union by decrea-sing the surgical insult. But the use of dynamic compression plating for these metaphyseal fractures led to metalwork failure, angular deformities and non-union.[7] All these ideas led to the evolution of the new plating system being broader distally to include more screw options for the small distal segment leading to better purchase of implant. The biomechanics of locking plates are designed to decrease the compressive forces between the plate and bone therefore decreasing the damage to periosteal blood supply. In contrast to the shear force with DCP these new plates convert axial loading into compression forces. Therefore locking plates are superior implants having better biomechanics especially in elderly osteoporotic bone and metaphyseal bone.[8] Another advantage of these LCP is the achievement of indirect reduction and use in bridging mode without compression. Percutaneous application of LCP causes less periosteal blood supply disruption and enhance early union. Hence pre-contoured anatomical locking plates for distal tibial fractures applied by MIPO technique results in higher union rates decreased wound complications and show better functional outcome.[10]

The motive of this study was to ascertain the radiological and functional outcome of distal tibial metaphyseal fractures treated by pre-contoured locking compression plates using minimally invasive percutaneous osteosynthesis (MIPO).

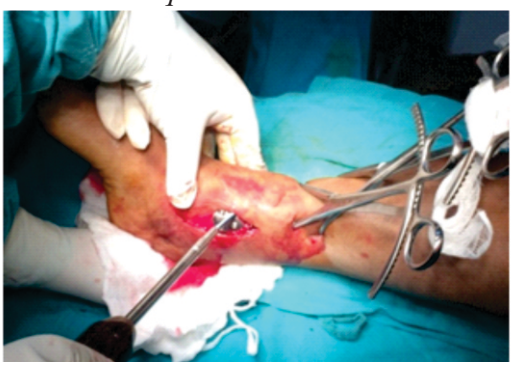
Material and Method

This was a prospective study conducted in the Department of Orthopedic Surgery, Services Hospital, Lahore from 2016 to 2018. We included 58 patients with closed distal tibial fractures according to AO classification 43A (A1, A2, A3) of either gender. Patients with associated vascular diseases, pathological fractures and compartment syndrome were excluded from the study. Review board of the hospital granted ethical approval for the study. Procedural benefits and risk were explained to the patients and informed written consent was obtained.

Initial management included fracture splinting, limb elevation and analgesia. All the patients underwent surgery by same surgical team using minimally invasive percutaneous plate osteosynthesis (MIPO) under image intensifier. Fracture reduction was done under C-arm with point reduction clamps. A 3cm incision was given medially distal to fracture site and with the help of periosteal elevator a tunnel was made for plate. Second incision was made around the proximal part of plate. **(Fig-1)** A minimum of 4 screws were placed proximal to fracture site. Anatomically pre-contoured locking compression plate was used in all cases. Anatomical reduction was achieved after plate insertion and screws placed by stab incisions. Range of movement exercises at ankle and knee initiated on 1st day after surgery. All patients were discharged to home by 3rd post-operative day. All patients were followed up after 2 weeks of surgery for wound examination and removal of stitches. Patients were later followed up at 06 weekly interval for assessment of bone union and functional outcome. Though range of motion exercises were started immediately post operatively, but weight bearing was commenced only after visualizing callus bridging fracture site. Functional outcome assessed by Tenny & Wiss criteria 100 points. Scores were graded as Excellent (>92), Good (87-92), Fair (65-87) and Poor (<65). Hammer et al criteria for bone union was used for radiological union. The criteria had five grades depending on the stage of bone union. Grade 5 fracture shows no callus or sign of union whereas Grade 1 denote Homogeneous bone formation with obliterated fracture line. We regarded Grade 3 as a minimum acceptable criterion for labelling union. **(Fig-2)**

The data was compiled and analyzed using SPSS version 19.0. Descriptive statistics was used. Quantitative data was like age, union time was presented as mean and standard deviation. Qualitative data like gender was presented as frequencies distribution. For categorical data Chi square test was applied and p-value <5 was taken significant.

Fig-1: *MIPO Technique*



Post operative AP & Lat view

Radiological union achieved

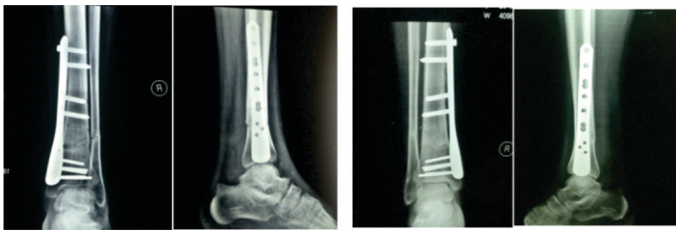


Fig-2: *X-Rays showing fracture distal tibia fixed with MIPO technique.*

Results

A total 58 patients with closed distal tibial metaphyseal fractures (43A AO classification) were enrolled. There were 46 (79.3%) male patients and 12 (20.7%) female patients. The male to female ratio was 4:1. Minimum age of the patients was 25 years whereas maximum age was 45year, with mean age of 34.12 years ± SD 5.98 years. Regarding the mechanism of injury 46 (79.3%) fractures were because of road traffic accident and 12 (20.7%) had history of fall. (Table-1) Functional outcome according to Tenny & Wiss 100 points Criteria was evaluated at 6 weeks intervals. Results were graded as Excellent > 92 points, Good 87 – 92 points, Fair if points 65- 87 and below 65 was graded as Poor outcome. The scores improved significantly after 6th week; 37 63.79%) patients achieved excellent and 18(31.03%) had good outcome at 12th week. At 24th week final follow-up 48 (82.75%) patients had excellent, 06 (10.35%) had good and 04 (6.90%) patients had fair outcome. (Table-2) In this study radiological outcome was assessed with the help of Hammer et al criteria. Grade 3 or apparent bridging of the fracture line was minimum requirement to be labelled united. At 24th week 49 patients had Grade-I, 7 patients had Grade-II and 2 patients radiological union was at Grade-III. The average time for union was 16.5 weeks with a range of 12 to 23 weeks. A 5 degree or more angulations in any plane (varus, valgus, procurvatum and recurvatum) was regarded as malunion. All the fractures united with acceptable alignment with no malunion.

Three patients developed superficial wound infection and were managed with one-week course of antibiotics. One of these patients was diabetic on oral hypoglycemic drugs with HBA1c level of 8.5. After opinion from Diabetic Management Center, she was shifted to insulin for proper control. Fortunately, infection was controlled in all patients and no further management was required.

Discussion

Table 1: *(General Statistics)*

1	**Age of patients**	**Average: 34.12±5.98** **Range: 25 years to 45 years**
2	Male : Female	4:1
3	Mechanism of Injury	Road Traffic Accident: 46 (79.3%) Fall: 12 (20.7%)

Table 2: *Functional Outcome Tenny & Wiss Criteria*

	6Th Week	12th Week	18th Week	24th Week
Excellent (>92)	0(0%)	37(63.79%)	41(70.69%)	48(82.76%)
Good (87-92 points	0(0%)	18(31.03%)	11(18.97%)	6(10.34%)
Fair (65-86 points)	0(0%)	3(5.17%)	6(10.34%)	4(6.90%)
Poor (<65 points)	58(0%)	0(0%)	0(0%)	0(0%)

Table 3: *Radiological Outcome*

Hammer et al Criteria	6th Week	12th Week	18th Week	24th Week
Grade-I (Excellent)	0(0%)	13(22.41%)	33(56.90%)	49(84.48%)
Grade-II (Good)	0(0%)	36(62.07%)	16(27.59%)	7(12.07%)
Grade-III (Fair)	0(0%)	9(15.52%)	6(10.34%)	2(3.45%)
Grade IV & V (Poor)	0(0%)	0(0%)	3(5.17%)	0(0%)

The ideal management of distal tibial metaphyseal fractures remains a riddle irrespective of extension into the adjacent ankle. The conventional treatment strategies are associated with unacceptable high complication rates. Intra-medullary nailing considered gold standard for diaphyseal fractures but not the best choice in distal metaphyseal fractures of tibia due to extremely short distal segment and mismatch between nail and tibia diameter. Traditional plating requires tremendous soft tissue trauma and periosteal stripping which further disrupt the blood supply. Therefore it was troubled by high risk of non-union, delayed union and wound complications.[11] Similarly, the use of external fixation for these fractures is associated with pin loosening in approximately half of the cases, pin tract infection, joint stiffness and significantly high percentage of mal-union. Evolution of minimally invasive technique (MIPO) had granted biological advantage of preservation of blood supply and decreased soft tissue problems. Pre contoured locking compression plates act synergistically with MIPO tech-

nique to provide a stable construct and bridled the common complications of internal fixation. These anatomically pre contoured plates also help to attain indirect reduction. Insertion of these newer implants requires a small incision and plates are tunneled extra-periostealy on the medial side of tibia. The enhanced screw options for distal fragment increase the stability of this fixed angle device.[12-15]

S. Hazarika reported his experience with MIPO for twenty tibial metaphyseal fractures with main focus on union time and related complications. He extended the indications to include open fractures in his study as well. Eight patients in his open fracture group achieved union within six months, while two cases of non-union were reported. In closed fracture group 7 patients achieved union in 6 months and no reported non-union. In his study 3 patients underwent implant removal because of deep surgical site infection and delayed wound dehiscence.[9] Implant failure was documented in one case at 32 weeks who had a redo surgery with DCP and union achieved. Whereas in our study we had two cases of superficial wound infection but no wound breakdown. Both the cases were successfully managed with oral antibiotics. Also, all our patients achieved union without any further intervention. Abid Mushtaq in a similar study used LCP with MIPO to fix twenty one distal tibial metaphyseal fractures. Average union time reported was 22 weeks (range 3–13 months). One case in his study required second surgery for non-union and finally union documented. Functional outcome was good in his 17 patients. Although two of his subject had superficial wound infection but no surgical intervention was required and fractures united.[6] The union time in our study was significantly lower 16.5week (range 12 – 23 weeks). The rate of infection in our study was 5.0% as compared to 10% in this study. In another study B Ganesh Bahadur Gurung union rate was reported to be 100% by 24th week. Full weight bearing was allowed in 93% cases at 24th week. Surgical site infection complicated two cases while another required bone grafting and fibulectomy.[16] The findings of this study match our results.

In his study Syah Bahari reported mean union duration of 22.4 weeks. Union rate was 100% with no case of non-union or mal-union. Infection troubled his three patients, deep in one while superficial in remaining two cases.[17] He utilizes SF 36 and AOFAS score to determine functional outcome. At 19th month follow-up mean SF 36 score was 85 whereas 90 was mean AOFAS score in his patients. These results are consistent with the results of our study with 54 patients (93.10%) showing excellent or good results at 24th week. Tenny and WISS criteria is 100 point system similar to AOFAS score with 50 point for pain and remaining 50 for the functional assessment, checking every aspect of functional outcome in complete detail.

The results of our study are comparable in fact better than other studies. The difference in union time among the studies could be because of the different criteria used for defining union. Functional outcome was excellent or good in > 90% cases irrespective of which scale they used. The soft tissue complications and malalignment risks encountered with other fixation techniques are minimized. These plates can be applied as neutralizing, compression or bridging implant. The choice mainly guided by the fracture geometry. For non-comminuted simple fractures reduction followed by lag screw and application in neutral mode or using plate as compression device. However there use as a bridging implant is more suitable for complex comminuted fractures. Rationale decision making and judicious use of pre-contoured LCP by MIPO increases the probability of union and are associated with fewer side effects.

Conclusion

In conclusion, MIPO using low profile pre contoured LCP for distal tibial metaphyseal fracture is a better implant choice due to high bone union and less complications. The newer implants and techniques have achieved this by minimizing the surgical insult, preserving precious periosteal blood supply and osteogenic fracture hematoma.

Conflict of Interest None

Funding Source None

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Authors Contribution

MA: Conceptualization of Project
MTJ: Data Collection
RDN: Literature Search
SAQ: Statistical Analysis
OIC: Drafting, Revision
SR, OA: Writing of Manuscript

Comparison of Efficacy of Methotrexate Versus Acitretin in the Treatment of Chronic Plaque Psoriasis

Shanze Shafiq,[1] Saadiya Siddiqui,[2] Amna Arif,[3] Shahbaz Aman[4]

Abstract

Objective: To compare the efficacy of methotrexate versus acitretin in the treatment of chronic plaque psoriasis

Method: Randomized Controlled Trial conducted in Dermatology Department, Services Hospital Lahore, on 60 patients after informed consent,divided into two groups. Group A was given methotrexate 0.3-0.5mg/kg orally and Group B was given acitretin 0.4mg/kg orally. Efficacy was ascertained by reduction in PASI score, calculated at baseline and at 12 weeks

Results : Patients of Group A achieved a reduction in PASI score from baseline 13.13±2.047 to 6.20±2.024 (efficacy76.7%) while in Group B, PASI score dropped from 13.53±2.047 to 7.00±1.857 (efficacy 56.7%) . Adverse effects for both groups were minimal.

Conclusion: Both methotrexate and acitretin are highly effective drugs in treating chronic plaque psoriasis. However, methotrexate showed greater efficacy and faster reduction in PASI as compared to acitretin.

Keywords: Efficacy, Methotrexate, Acitretin, Chronic Plaque Psoriasis

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Introduction

Psoriasis is a common, chronic, inflammatory condition of the skin, characterized by red, scaly, sharply demarcated, indurated plaques, present particularly over the extensor surfaces of the skin and scalp. The disease varies in its graveness over time and in individuals during life. It is polygenic in predisposition and is influenced by environmental triggers such as trauma, infection, or medication.[1]

Psoriasis is prevalent in different populations varying from 0.27% to 11.4%, more common in high income countries and elderly, often presenting in bimodal distribution, in both genders ,with women affecting a little earlier than men.[2]

Psoriasis Area and Severity Index (PASI) is used to assess the severity of psoriasis. We scan four areas of the body (head, trunk, upper and lower limbs) in relation to erythema, induration (thickness), desquamation (scaling) of the plaques and body surface area involved. Scores are assigned from 0 to 4 based on intensity of erythema, induration and scaling to figure out severity of psoriasis.[3]

Oral methotrexate, an antimetabolite, is an effective immunomodulator used for treating psoriasis over. The drug competitively inhibits enzyme dihydrofolate reductase resulting in lower nucleic acid production through folate, in a dose dependent manner. Low dose weekly administration inhibits proliferation of lymphoid tissue in psoriatic plaques.[5]

The oral retinoids are vitamin-A derivatives , possess immunomodulatory and anti-inflammatory activity, used for treating psoriasis. The drug modulates epidermal proliferation and differentiation. Etretinate was the first retinoid introduced now replaced by acitretin which is its active metabolite.[4]

Naldi et al., studied methotrexate in chronic plaque

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psoriasis and reported a reduction of 75% in their PASI score values.[6] In Pakistan Sabiqa et al., recorded an almost complete remission in 40% of patients during eight weeks of treatment with methotrexate at a dosage of 7.5mg weekly.[7]

Borghi A et al., reterospectively evaluated the efficacy and safety of acitretin in moderate to severe plaque psoriasis concluded that acitretin at an initial low(10 mg/day, gradually increased (<50 mg/day) than maintaining at the minimal effective dose, is a suitable treatment option for plaque psoriasis.[8] Acitretin in combination with TNF-α monoclonal antibodies has a synergistic effect alleviates secondary no response to the biologics, improves drug efficacy, accelerate the remission and reduce the costs of disease reduces the incidence of cardiovascular events and mortality.[9] While comparing both drugs with each other Noor SM et al., found excellent response with methotrexate in 53.5% against 25.3% in acitretin group in chronic plaque psoriasis.[10]

Therefore ,we have conducted this research in our set up to find out which drug is more efficacious among the two, thus enabling healthcare professionals in developing a good treatment protocol for the disease with profound psychosocial impact.

Methods

This randomized controlled trial was carried out in the Dermatology Department, Services Hospital Lahore in total sixty patients, of either gender and age ranging from 18-50 years suffering from chronic plaque psoriasis, of any duration with PASI ≥10 were enrolled through non probability convenient sampling and equally divided into two groups of 30 patients each.

Psoriasis: Patients having characteristic erythematous, scaly, indurated lesions over extensor surfaces of the skin, with PASI≥10. Patients suffering comorbidities like eczema, lichen planus, systemic illnesses like chronic liver disease, lung disease, anemia, alcoholics, drug allergy, using any topical treatment within 2 weeks, or systemic therapy before 4 weeks of study, pregnant or lactating female ,having abnormal lipid profile (cholesterol more than 230md/dl and triglycerides more than 200mg/dl) or suffering from Hepatitis B/Hepatitis C/ HIV were excluded. Distributed into two groups A and B using lottery method. An antimetabolite, administered to group A in the form of a tablet 0.3-0.5mg/kg, orally once a week for 12 weeks. Tablet folic acid 5mg once daily was given to patients to mini-mize systemic side effects. Vitamin A derivative, administered to group B, as a capsule 0.4mg/kg orally, daily for 12 weeks. Efficacy was assessed as a reduction in PASI score which was assessed at baseline and the completion of study 12 weeks later. Drug was considered efficacious if the reduction in PASI from baseline will be ≥50%.

$$\% \text{ Reduction} = \frac{\text{Baseline PASI - Post-treatment PASI}}{\text{Baseline PASI}} \times 100$$

Efficacy was assessed at baseline and after 12 weeks. Information regarding demographic data and outcome variables recorded in a predesigned proforma. Data was analyzed using SPSS version 22. Quantitative variables like age and duration was assessed as mean ± standard deviation. Both groups were compared using the chi-square test. Qualitative variables like gender and efficacy was presented as frequency and percentages. Effect modifiers such as age, gender and disease duration were controlled by stratification. Post stratification chi-square test was applied to compare the two groups. P-value of ≤0.05 was taken as significant.

Results

A total of 60 patients were enrolled in the study. The mean age of the patients was 30.73±6.62 years with minimum and maximum age of 19 and 50 years respectively. Among patients from Group A, the mean age of the patients was 29.50±6.85 years, whereas the mean age of patients in Group B was 31.97±6.26 The number of male patients in the study was 26(43.33%) while 34(56.67%) patients were females. **(Fig-1)** In our study 33(55%) patients were married while 27(45%) patients were unmarried. Mean duration of disease of the patients was 10.15±4.51 months with minimum & maximum duration of 2 & 60 months respectively. In Group A, the mean PASI score at baseline was 13.13±2.047 which reduced to mean PASI value of 6.20±2.024 at the end of 12 weeks with a mean percentage reduction of 53.46± 10.64. In group B, mean PASI at baseline was 13.53± 1.717 which reduced at 12th week follow up to the mean PASI score of 7.00±1.857 with mean percentage reduction of 48.24±12.24. (Table 1) According to this study, efficacy was achieved in 40(66.67%) of the total 60 enrolled patients. **(Fig-2)** In the methotrexate group the efficacy achieved in 23(76.7%) patients. Among acitretin group the efficacy achieved in 17(56.7%) patients. Statistically both group showed insignificant difference. i.e. p value=0.100.**(Table -2)** According to the age stratification, in patients with age ≤ 30 years, efficacy in methotrexate group was achieved in 15(78.9%) patients (p value=0.055) and in acitretin group it was achieved in 6(46.2%) patients. In patients with age > 30 years, in

methotrexate group, efficacy was achieved in 8(72.7%) patients (p-value=1.00). Among acitretin group the efficacy achieved in 11(64.7%) patients.**(Table-3)** The study results showed that in patients with duration of disease ≤ 8 months, in methotrexate group the efficacy was achieved in 7(70.0%) patients, whereas in the acitretin group, the efficacy was achieved in 8(72.7%) patients (p-value=0.890). Similarly in patients with duration of disease >8 months, in methotrexate group the efficacy achieved in 16(80.0%) patients, and among acitretin group the efficacy achieved in 9(47.4%) patients (p-value=0.048). **(Table -3)**

Table 1: *Summary statistics of PASI score at baseline and 12 weeks along with percentage reduction between study groups*

PASI	Study group		p-value
	Methotrexate 30	Acitretin 30	
Baseline	13.13±2.05	13.53±1.72	0.415
12th week	6.20±2.02	7.00±1.86	0.116
Mean Percentage reduction	53.46	48.24	0.083
Standard deviation	10.64	12.24	

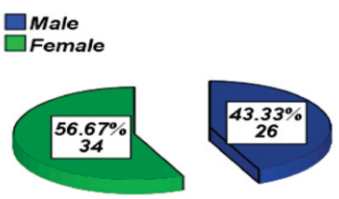

Fig 1: *Distribution of Gender in Study Population*

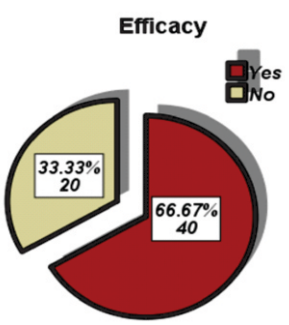

Fig 2 : *Distribution of Efficacy in Study Population*

Patients on methotrexate varyingly experienced nausea, headache, body aches, vertigo managed with medication. Acitretin group suffered from pruritis, mucocutaneous dryness, cheilitis, but none required treatment discontinuation.

Table 2: *Distribution of efficacy between study groups*

Efficacy	Study Group		Total	p-value
	Methotrexate	Acitretin		
Yes	23	17	40	0.100
	76.7%	56.7%	66.7%	
No	7	13	20	
	23.3%	43.3%	33.3%	
Total	30	30	60	
	100.0%	100.0%	100.0%	

Table 3: *Distribution of efficacy between study groups according to age and duration of disease*

Age (years)	Efficacy	Study Group		Total	p-value
		Methotrexate	Acitretin		
⩽ 30	Yes	15	6	21	0.055
		78.9%	46.2%	65.6%	
	No	4	7	11	
		21.1%	53.8%	34.4%	
>30	Yes	8	11	19	1.000
		72.7%	64.7%	67.9%	
	No	3	6	9	
		27.3%	35.3%	32.1%	
Duration of disease (months)					
⩽ 8	Yes	7	8	15	0.890
		70.0%	72.7%	71.4%	
	No	3	3	6	
		30.0%	27.3%	28.6%	
>8	Yes	16	9	25	0.048
		80.0%	47.4%	64.1%	
	No	4	10	14	
		20.0%	52.6%	35.9%	

Discussion

Psoriasis is a chronic skin disease. Mild disease is usually controlled with topical treatment while for moderate severe condition phototherapy, methotrexate, acitretin, ciclosporin, apremilast and biologic therapies (e.g., etanercept, infliximab, secukinumab) are good options. Combination drug therapy is used depending upon short and long-term considerations, disease severity, efficacy and side effect profile of available treatment options, quality of life of the patient and affordability.[11]

Our study results showed that both methotrexate and acitretin were effective as evident by the decreasing scores for psoriasis area severity index, once treatment started. But after 12 weeks of treatment, methotrexate was found to be more effective of the two with a greater number of

patients achieving efficacy.

The mean age of the patients in our study was 30.73± 6.62 years with minimum and maximum age of 19 and 50 years respectively. This was very similar to the mean age of 35.14 ± 16.[16] years that was found in a study by Affandi et al, as part of a 10 year review of Malaysian Psoriasis registry.12 Psoriasis is bi-modal with two age brackets with first peak occurring at 16-22 years, and the second at 57-60 years[13]. This was not found in our study, but our results were consistent with other study conducted in Taiwan, in which psoriasis was seen in the third decade of life.[14]

Our study population consisted of 26 (43.33%) male and 34(56.67%) female patients. The greater percentage of females reported is perhaps due to greater feelings of stigmatization related to disease and being more strongly impacted psychologically. Women are affected more with psoriasis; feeling unhappy (women: 18.5%; men: 11.3% lower vs. general population), stressed (women: > 60%; men: 42%), socially isolated (women: 25-28%; men: 19-24%), stigmatised (Feelings of Stigmatization Questionnaire score; women: 93.2; men: 78.0), and reduced libido (women: 33%; men: 19%) compared with men.[15] That is why more women chose to seek treatment for their psoriasis in our study. In another study by Gawlik et al.,16 out of a total of 130 patients, 56.92% (70) were female. The gender distribution in this study is closer to our own. While some other studies indicated males to be affected more in Germany[17] (0.76% vs 0.66%), and in United States[18] [2.5% vs 1.9% with an odds ratio=1.37 (95% CI: 1.14–1.64). Of the total 60 patients in our study 33(55%) were married while 27(45%) patients were unmarried. Although more married chose to seek treatment in our study but in a study done by Gawlik et al., where 59.23% of the respondents were married. The impact of psoriasis was more profound in single individuals. Marital status disturbs Quality of Life (QoL) with important statistical difference among married Vs unmarried statuses (Kruskal–Wallis test: $\chi 2 = 10.411$; df = 3; p = 0.034).[16] As such, marital status may influence which patients choose to seek treatment.

Mean duration of disease in patients was 10.15±4.51 months in our study. This was very low in contrast to what noted by Colombo et al., in Italy where the mean time of disease duration was 18.7 years. This difference can be due to the fact that the study from Italy recruited psoriasis of all severity and there was no minimum body surface area involvement, whereas in our study, a minimum of 10% of BSA (Body Surface Area) involvement was required for eligibility.[19] It is possible that patients with greater area severity sought treatment earlier in the course of disease.

Regarding PASI, patients in the methotrexate group had a mean PASI of 13.13±2.047 (p-value=0.415). At week 12, the mean PASI score was 6.20±2.024 (p-value = 0.116). In this group, the mean PASI reduction from baseline to week 12 was 53.46±10.64%.

For those in the acitretin group, the mean PASI score at baseline was 13.53±1.717(p-value=0.415), which had dropped to a mean of 7.00±1.857 (p-value= 0.116) at week 12. The mean percentage reduction in PASI was 48.24±10.24%.

Efficacy was achieved in 76.7% (23) of patients in the methotrexate group, whereas in patients being given acitretin, 56.7%(17) patients achieved a 50% or greater reduction in PASI compared to baseline. Statistically both groups showed insignificant difference. i.e. p value = 0.100.

In a study by Naldi et al., it was concluded that use of methotrexate resulted in clinical improvement of 75% of patients, which is comparable to the results of our study.[6] Similarly, Sabiqa Haider et al., found that methotrexate satisfactorily controlled disease within 5-7 weeks (mean 6±0.89 weeks).[7] The mean baseline PASI reduced from 14.8±4.2 to 4.9±4.3(reduction in PASI of 95%) in 29(40%) patients. Partial remission (reduction in PASI of 75%) was achieved in 44 (60%) patients. In our study, 76.7% of patients of methotrexate were able to achieve a 50 percent or greater reduction in PASI scores. This is greater than the 60% of patients that were able to achieve a partial remission in the study by Sabiqa et al., possibly because a different end point was used. We declared the drug efficacious at 50% reduction in PASI from baseline whereas the other study in question used a 75% reduction in score from baseline to declare partial remission. Hence, the results are comparable. In another study by Heydendael et al., partial remission was achieved by 60% of patients on methotrexate after 16 weeks of treatment. The end point employed by this study was also a 75% reduction in PASI score from baseline, which was higher than the percentage reduction used in our study.[20]

In our study, 56% of patients achieved efficacy on acitretin. The result is comparable to Murray et al., who observed a response in 60% of the patients.[21]
According to a study conducted by Parsam et al., com-

paring methotrexate versus acitretin in palmoplantar psoriasis, concluded that oral methotrexate clears condition faster than acitretin with statistically significant reduction in scores .The MPASI score in group I was 57.15 ± 17.17 at baseline and 14.50 ± 13.55 at the end of 3rd month. While MPASI score in group II was 57.76 ±18.60 at baseline and 21.30 ± 8.168 at the end of 3rd month.[22] The study results were very close to our own, which could be due to the fact that our sample size and doses of methotrexate and acitretin used in both studies were very similar.

Noor et al., conducted a study in Pakistan comparing the efficacy of methotrexate and acitretin in the treatment of chronic plaque psoriasis. They concluded that methotrexate is a better option than acitretin for patients of moderate to severe chronic plaque psoriasis. In their study of 142 patients, 53.5% of patients achieved an excellent response (PASI75) on methotrexate while 25.3% of patients on acitretin were able to achieve an excellent response.10The results are in line with our study, as a greater percentage of patients on methotrexate were able to achieve efficacy compared to those on acitretin.

Conclusion

From our present work we conclude that both methotrexate and acitretin are efficacious in treating chronic plaque psoriasis and can be used alone or in combination with other therapies especially biologics to achieve sustained remission. These drugs are cost effective alternatives to expensive biological therapies.

Conflicts of Interest *None*

Funding Source *None*

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Authors Contribution

SS: Conceptualization of Project
SS, AA: Data Collection
SS, AA: Literature Search
SS: Statistical Analysis
SS: Drafting, Revision
SS: Writing of Manuscript

Comparison of Writing Patterns of Prescription in Public and Private Sector Hospitals in Multan

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Abstract

Objective: To compare and evaluate handwritten prescriptions from the public and private sector hospitals/clinics and to determine whether there is any significant difference between the two.

Method: This study was Hospital based cross-sectional study. Study was conducted in the Department of Pharmacology and Therapeutics, Nishtar Medical University for a period of 3 months post-approval (June 2022-August 2022).Total 400 prescriptions were part of this study with 200 from private and 200 public hospital. They were collected and assessed under the World Health Organization's Guide to Good Prescribing. The prescriptions from one sector were then compared against those from the other sector to identify any significant differences.

Results: All prescriptions lacked at least some of the criteria of a good prescription with prescriptions from the private sector being better than those from the public sector. Prescriptions from both sectors were almost completely deficient as regards to the use of generic drug names. There was negligible difference between both sectors in terms of legibility of written prescriptions (p=0.057). While name of patient, his/her age, address, vitals, drug strength, dosage, and total quantity of drug prescribed are were compared, there were significant differences of 0.032, 0.021, 0.039, 0.048, 0.041, 0.033, and 0.039 respectively.

Conclusion: The private sector executes better than the public sector in prescription writing, but both sectors so far have fall short of the standards set by the World Health Organisation.

Keywords: prescription writing, prescription errors, private sector, public sector, prescription guidelines

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Introduction

A prescription is a set of instructions issued by a registered medical practitioner to a pharmacist to provide the patient with medication.[1] It should include information about dose, route of administration and the duration of drug administration, the goal of which is to improve a patient's quality of life.[2] Concise and accurate prescriptions have the effect of shortening the duration of a patient suffering from a disease or a debilitating condition. It should be written in a very clear, legible manner, without unofficial abbreviations and it must follow the legal requirements of a prescription.[3] Different countries may follow different patterns of writing a prescription, but they all follow some common standard points which include: the patient's demographic details, information about the drug (i.e., form of drug, frequency of intake, dose, concentration, manner of administration, duration of treatment with prescribed drugs) and data of the physician prescribing these drugs.[4] The key factors in a well-written prescription are not only limited to the efficacy of the prescribed drug, the mode and duration of drug administration/application

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but also include a precise diagnosis, patient's vital information (weight, temperature, heart rate, etc) and potential toxic effects of the medication.

Absence of any of these components will lead to errors of prescription and ultimately will have reduced effectiveness of treatment on patient's health.[5] According to a World Health Organisation (WHO) report, 50% of all medication is needlessly dispensed which is a waste of resources.[6,7] WHO has formulated some indicators to measure the drug performance and to evaluate prescription (i.e., errors of omission and commission). Errors of prescription are of two types: a prescription that is deficient in essential information (i.e., inadequate information about dose strength, form of intake, quantity of drug and duration of drug to be delivered) contains the "error of omission". An error which occurs due to incorrectly written prescription is called "error of commission". Both errors can be avoided if a prescription is written following specified standards of writing. Both errors make treatment ineffective which leads to a wastage of time and resources and negatively impacts a patient's health and well-being. A study demonstrated that more than 15% of the prescription errors occur because of illegible prescription writing, unfamiliar abbreviations, problems with the zeroes position in the dose and incomplete drug instructions.8 Unfortunately, in Pakistan prescription writing remains unchecked by health authorities and is not given much importance. This ultimately causes patients to use drugs inappropriately which may adversely affect their health.[9]

An audit is defined as assessment of a method or a quality system that compares the existing system in contrast to its defined standards in order to point out its differences from the approved criteria and improve the quality of the actual process. Prescription auditing is a quality improvement process for enhancing the quality of patient care through a systematic review according to the recommended criteria and if done on the regular and strict pattern, it can improve the quality of treatment for the patient and ultimately setting high standards of health facilities.[10]

Materials and Methods

It was a hospital (outpatient) based cross-sectional study conducted in the department of Pharmacology and Therapeutics, Nishtar Medical University. Outpatient clinics, both at government and private sector hospitals, in Multan and its suburbs were the location where prescriptions were collected. Ethical approval was obtained from the Ethics Review Committee Nishtar Medical University and the duration of the study was 3 months post-approval from the committee. 400 samples were collected at random, with 200 samples collected per sector (government and private sectors). Only handwritten prescriptions of consultant doctors (FCPS, FRCS, or an equivalent degree) were included in this study and prescriptions that were typed or printed were excluded. Prescriptions written by post graduate residents and medical officers were also excluded. A double-blind cross-sectional study was carried out where prescriptions provided to patients at both government (public) and private hospitals/clinics were collected for research purposes. In this randomised study, the prescriptions were analysed under WHO Guide to Good Prescribing and data was entered into a table containing all the requirements for a complete and legible prescription under WHO guidelines. The table contained details about the patient, the prescriber and details of the medications prescribed. Data about patients contained their name, age, address, gender, vital information (blood pressure, heart rate, weight, oxygen saturation, height) and the date they visited the hospital. Prescriber's details covered the name, address, and phone number at which a patient may contact the doctor. Drug details included generic drug name, strength of the drug, dosage form, and total amount of drug to be prescribed. Instructions/warnings regarding the drug(s) prescribed were also included and the prescription was also assessed regarding its legibility. Confidentiality of the patients and doctors involved was strictly maintained.[10] The obtained data was analysed using SPSS version 23. WHO Prescription writing criteria falls in quantitative parameter and it was compared through independent t test. Probability value less than 0.05 was considered statistically significant ($p < 0.05$).

Results

While neither sector precisely followed WHO guidelines for prescription writing, prescriptions obtained from the private sector conformed more to the guidelines than those obtained from the public sector. Prescriptions mentioning date of treatment in the public sector (n=131, 65.5%) were lower than the private sector (n= 183, 91.3%). Regarding the demographic details of the patients, the name and age of the patients treated in the public sector were mentioned on 93.4% (n=187) and 39.3% (n=78) of the prescriptions respectively. In the private sector, this figure stood at 96.5% (193/200) and

89.6% (179/200) for patient name and age respectively. While prescriptions from the private sector mentioned gender in 86.2% (n=172) of the prescriptions (18% in public sector prescriptions, n=36), they lagged as compared to the public sector in noting down the address of the patients 8.6% (n= 17) in private sector as compared to 31.1% (n=62) in public sector. Only 11 % (n=22) of the prescriptions in the public sector had the patient's vitals. In the private sector this criterion stood at 55.2% (n=110). In regards to prescriber biodata, 77.0% (n=154) mentioned the prescriber's name in the public sector compared to 79.3% (n=159) in the private sector. Address of the prescriber was mentioned in 70.4% (n=141) of public sector prescriptions with none of the prescriptions providing a contact number if a patient needed to contact the prescribing physician. On the other hand, private sector prescriptions contained a phone number and prescriber's address in 98.2% (n=196) of the prescriptions. This can be attributed to physicians using hospital letterhead to write down the medicine; these have the address and phone number of the hospital printed on them. WHO guidelines prescribe that medicine be prescribed under its generic name. In the public sector, drugs were prescribed under their generic names in 1.6% (n=3) of prescriptions and in 5.1% (n=10) of the private sector prescriptions. The private sector mentioned the dosage form in 100.0% (n=200) of prescriptions while public sector mentioned it in 85.2% (n=170). In the public sector, strength of drug and total amount of drug(s) prescribed stood at 70.4% (n=141) and 55.7% (n=111) respectively. The private sector prescriptions had these values at 53.4% (n=107) and 32.7% (n=65).

Table 1: *Comparison of Prescriptions of Public and Private Sectors.*

Variable	*p*-value
Name of Patient	0.032
Age of Patient	0.021
Address of Patient	0.039
Gender of Patient	0.029
Patient's Vitals	0.048
Generic Drug name	0.067
Strength of Drug	0.041
Dosage form	0.033
Total amount of Drug	0.039
Label: Instructions/Warnings	0.031
Legibility of Prescription	0.057
Name of Prescriber	0.019
Address of Prescriber	0.025
Telephone of Prescriber	0.036

There was no significant difference in the legibility between prescriptions from both sectors with public sector prescriptions legible at 63.9% (n=128) and private sector at 63.7% (n=127) of prescriptions. Meanwhile instructions/warnings (paired together) were mentioned in 83.6% (n=167) of public prescriptions and 89.6% (n=179) of private prescriptions.

With a p-value of less than or equal to 0.05 being significant, it can be seen from data provided in the table 1 that there were significant differences between prescriptions obtained from the private and public sector (except for legibility). There were no significant differences between the sectors as regards to legibility of the prescriptions and usage of generic drug names to prescribe medication. With regards to prescriber and patient biodata, the private sector fared better than the public sector. Only in the criterion of patient's address did the public sector perform better than the private sector. Regarding the drug dosage, drug form, total amount of drug(s) to be consumed and strength of drug(s), the private sector outperformed the public sector. Private prescriptions provided more instructions and warnings as regards to drug consumption than the public sector. Overall, it can be easily identified that the private sector performed better than the public sector in prescription writing.

Discussion

Prescriptions were examined under WHO guidelines for prescription writing. The main criteria upon which pharmacists can provide patients with medication is legibility of the prescription. In this study, a prescription was classed as illegible when one or more drugs in the prescription were illegible to the author. Though subjective, illegible prescriptions accounted for 36.2%, compared to 23.9% of prescriptions analysed in a study conducted in India.[11] Illegible handwritten prescriptions obtained in a study in Saudi Arabia were at 14.88%.[12] In our study, 5.1% of prescriptions from the private sector (private prescriptions) contained drugs under their generic names, as compared to 0% from the study Phalke and colleagues.[11] Date the prescription was issued on was mentioned in 65.5% and 91.3% of public and private prescription samples respectively. This is higher as compared to a study of prescription writing conducted in Saudi Arabia by Irshahid where the date was mentioned in 35.7% of prescriptions.[13] Prescriptions analysed made no mention of any potential drug interactions nor did they mention the registration number of the physician who wrote the prescription. The most

common patient biodata error was of the patient vitals with 88.5% of public sector prescriptions (public prescriptions) missing this data, while in a study conducted in Al-Qassim, Saudi Arabia, this figure stood at 34.27%.[12] Patient vitals, especially weight, are important for children and elderly as this affects pharmacokinetics and pharmacodynamics of prescribed drugs. Drug dosage was mentioned in 85.2% of public prescriptions and 100% of private prescriptions. This is a higher rate when compared to a study conducted in Peshawar, Pakistan where the dosage was mentioned in 63.8% of the prescriptions and directions for drug usage were mentioned in just 10.9%.[14] In comparison, our study found that instructions/warnings (grouped together for convenience) were mentioned in 83.6% of public and 89.6% of private prescriptions. Our study found that just 8.6% of private sector prescriptions mentioned the patient's address. This makes it extremely difficult for hospitals to track patients in case of follow-up. In comparison, public prescriptions mentioned patient address in 31.1% of the cases. This is a slight improvement from a study conducted in Pakistan where the address was missing in 98.3% of prescriptions.[15] There was a lack of mention of age in public sector prescriptions, which could lead to the pharmacist being unable to verify the dosage of the drug which could lead to potential toxic effects in children and the elderly. Age of patient was mentioned in just 39.3% of public prescriptions but in 91.3% of private sector prescriptions. While a value of 100% would be ideal, our study ranked higher than the aforementioned study where the patient's age was mentioned on just 30% of the prescriptions. This study is a novelty study in being the first study to compare prescription writing practices in private and public sector hospitals/clinics in Pakistan. Our study shows that more prescriptions from the private sector had the hospital's address as compared to public sector prescriptions (p=0.025). This trend is supported by a study conducted in Nigeria where private sector addresses were mentioned more than public sector ones (p=0.005). It was also observed that patient's age was recorded more often in private hospitals than public hospitals (p=0.015). Our study concurred with this observation with (p=0.021).[16]

In our study, none of the prescriptions obtained from both sectors, public and private, were complete. Errors in prescription could be attributed to high patient volume at medical centres where physicians do not have the necessary time to fill out a prescription. A study conducted in China found that higher rates of prescription errors occurred when there was increased workload (p<0.001).[17] The most common error in prescriptions of both sectors was the lack of the usage of generic drug names. The lack of prescription of generic drugs may be attributable to patient belief that generic drugs lack efficacy and poor awareness regarding generic medication.[18] It may also be attributed to the rampant advertising by pharma companies of their brand drugs and offering incentives to doctors to prescribe these drugs. In a study conducted in Nepal, it was found that majority of the patients had poor health literacy and lacked awareness of generic medication. This was also found to be the case in medical students and interns and hence led to lower prescription rates of generic drugs at tertiary hospitals.[19] This place an unnecessary burden on the poor man who may not be able to afford the branded medication.

Conclusions

Prescription writing is dismal despite efforts to the contrary. The private sector performs better than the public (government) sector in prescription writing, but both sectors still fall short of the standards set by the World Health Organisation.

Conflict of interest *None*

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Authors Contribution

NI: Conceptualization of Project
SAM: Data Collection
AA: Literature Search
SG: Statistical Analysis
WB: Drafting, Revision
HP: Writing of Manuscript

Correlation of Visceral Fat with Anthropometric Indices and Cardiovascular Disease Risk Factors

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Abstract

Objective: To determine the correlation between visceral fat and body mass index (BMI), waist circumference (WC), waist-to-hip ratio (WHR), and CVD risk factors in males and females of the Pakistani population.

Method: Four hundred six (406) participants were enrolled in the study after taking ethical approval from the CMH LMC & IOD, Lahore. The age of the participants was 30 to 65 years. A uniform survey and physical examination were given to each participant. We took anthropometric measurements (BMI, WC, WHR, WHtR, SBP, and DBP). Fasting blood sugar and the serum lipid profile (TC, TG, HDL-C, and LDL-C) were measured.

Results: The participants with visceral fat $\geqslant$ 10% have increased levels of SBP, DBP, Cholesterol, LDL, TG, and FBS. A significant positive correlation between visceral fat was observed with Weight, BMI, WC, WHR, SBP, DBP, Cholesterol, TG, and FBS.

Conclusion: CVD risk increases with the increase in weight, BMI, WC, WHR, SBP, DBP, Cholesterol, TG, and FBS

Keywords: Visceral fat, CVD, HTN

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Introduction

Leading contributors to death and disability are cardiovascular disease (CVD) and diabetes. When a person has risk factors for one or both illnesses, it is known as metabolic syndrome.[1] It has at least 3 of the following five components: abdominal obesity, elevated triglycerides, decreased HDL and LDL cholesterol, hypertension, and impaired glucose regulation.[2] The glycemic imbalance which is linked to the risk of CVD is mainly brought about by an increase in the fat content of the body.[3] Obesity is described as having too much body fat. It is the outcome of a prolonged imbalance between food intake and energy usage. This mismatch has been growing year after year and has reached alarming proportions.[4] The World Health Organization (WHO) lists obesity as one of the most significant public health issues. Over 1.9 billion people worldwide were overweight in reports 2014. 600 million among them are already obese. Obesity and overweight increased by 47.1% and 27.5% respectively among children and adults from 1980 to 2013.[5] As per World Health Organization (WHO) gauges, cardiovascular illness prompts 31% of all passing worldwide whereas low and center pay nations contribute 82% of this weight.[6] There is a significant burden contributed by South Asian countries.[7] The number of inhabitants in the Indo-Pak subcontinent are among the populations with the most noteworthy dangers of CAD on the planet and which is

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the reason coronary vein sickness is the overwhelming reason for mortality among this population.[8] Pakistan is one of the emerging nations where the prevalence of overweight and obesity has multiplied. According to global disease estimates from 2014, Pakistan is ranked eighth among the 10 nations hosting 693 million obese people worldwide.[8] Major human organs like the liver, pancreas, and kidneys are typically wrapped by visceral body fat. It makes sure that there is room between each organ. Inflammation and high blood pressure are caused by excess visceral fat deposits which raises the risk of major health issues. High levels of visceral body fat, high blood pressure, and insulin resistance has been shown to cause interconnected abnormalities in non-diabetic men.[9] According to past research, regional fat distribution in moderate obesity appears to significant predictor of metabolic and cardiovascular risk. Studies have demonstrated a correlation between extra body fat in the upper body and higher chances of mortality as well as diabetes, hyperlipidemia, and hypertension. Even though the cause-effect relationship has not been shown, the research implies that body visceral fat may be a common component linking various aspects of metabolic syndrome, such as glucose intolerance, HTN, dyslipidemia, and insulin resistance.[10]

Blood pressure has been linked to visceral fat according to several studies.[11-13] Positive correlation between visceral fat (VF) and blood pressure has been shown in Caucasians, African Americans, and Japanese Americans in several cross-sectional investigations of the US population.[14,15] The prevalence of HTN and the relationship between visceral fat and blood pressure were seen in the Framingham cohort.[11] Excess body weight and high CV risk is the major challenge in many developing countries including Pakistan. The present study is done to determine the correlation of VF with anthropometric indices and CVD risk factors.

Material and Methods

Four hundred six (406) participants were enrolled in this cross-sectional study after receiving ethical permission from the institute of CMH LMC & IOD, Lahore. This study was conducted from October 2021-April 2022. Nonprobability convenient sampling technique was used. The sample size was calculated by using sample size calculator in health studies. Keeping the confidence level 95% with margin of error 10%, the calculated sample size was 406. Participants ranged in age from 30 to 65. Informed written consent was taken before recruitment of participants. Each participant received a standard questionnaire as well as a physical assessment. We measured anthropometric indices (BMI, WC, WHR, WHtR, SBP, and DBP). The serum lipid profile (TC, TG, HDL-C, and LDL-C) and fasting blood sugar levels were assessed. Statistical Software Package version 25 was used to enter the data. In the case of quantitative variables, mean±SD was used. The link between the variables was examined using the Pearson correlation coefficient. All tests were two-sided. A statistically significant difference was defined as a p-value< 0.05.

Results

Four hundred six (406) participants were enrolled. Among them, 39% were male and 61% were female. The mean age (SD) of female and males were 42.35 (±15.22) and 43.82 (±15.39) years, respectively. All study subjects were divided into two groups, persons having higher body visceral fat percentage (>10%) in one group and visceral fat within cut-off value (10%) in another group. The group having higher visceral fat had significantly higher mean values of body fat percentage, BMI, blood pressures, blood sugar levels, and almost all laboratory data than those in the low visceral fat group. There is a significant increase in SBP, DBP, Cholesterol, LDL, TG, and FBS in participants having visceral fat ≥ 10% (Table-1) A significant positive corre-

Table 1: *Distribution of participants based on body visceral fat percentage*

Variables	Total (means± SD)	V-fat⩽ 10%	V-fat⩾10%	P
Age (years)	37.39±12.25	35.33±11.61	48.02±9.74	⩽.001
SBP (mmHg)	124.23±16.21	121.44±14.02	138.64±19.02	⩽.001
DBP (mmHg)	82.67±13.17	80.37±11.61	94.52±1350	⩽.001
Cholestrol (mg/dl)	189.37±41±64	186.82±41.43	202.52±40.56	.005
LDL (mg/dl)	127.42±37.42	125.57±37.48	136.96±35.92	.02
Triglyceride (mg/dl)	162.17±67.92	158.36±66.98	181.81±69.83	.01
HDL (mg/dl)	43.54±9.12	43.262±9.47	43.14±7.14	0.6
FBS (mg/dl)	101.67±34.82	97.40±29.56	123.67±49±10	⩽.001

lation between visceral fat was observed with Weight, BMI, WC, WHR, SBP, DBP, Cholesterol, TG, and FBS. P-value for SBP is 0.000 and P value for DBP is 0.001 (Table 2) CVD risk increases with the increase in weight, BMI, WC, WHR, SBP, DBP, Cholesterol, TG, and FBS

Table 2: *Correlation of VF with anthropometric indices and CVD risk factor*

Variables		P
Age (years)	0.599	⩽. 001
Weight (kg)	.811	⩽. 001
Height (cm)	.002	0.9
BMI (KG/m^2	.837	⩽.001
WC (cm)	.800	⩽.001
WHR(cm)	.403	⩽.001
SBP(mmHg)	.499	⩽.001
DBP (mm Hg)	.511	⩽.001
Cholestrol (mg/dl)	.147	.003
LDL(mg/dl)	.094	.058
Triglyceride (mg/dl)	.209	⩽.001
HDL(mg/dl)	.024	0.6
FBS(mg/dl)	.346	⩽.001

Discussion

In this study, there is a significant increase in SBP and DBP (p≤ .001) in participants having visceral fat > 10%. A 12-week meal replacement strategy for men was observed to enhance SBP and DBP, and there was a favourable correlation between a drop in body visceral fat.[16]

Among Americans, body VF was significantly (p= 0.001) associated with Systolic and Diastolic BP, according to Fox et al.[11] However, only Visceral adipose tisssue provides useful information beyond BMI and waist circumference. Their research also showed a positive association between the prevalence of hypertension and both SAT (subcutaneous abdominal adipose tissue) and VAT (visceral adipose tissue). According to prior research, only VAT was linked to hypertension among Japanese Americans and whites, even after accounting for BMI and waist circumference[14,17], whereas both Subcutaneous and Visceral AT were associated with hypertension in both men and women among black[15], demonstrating the relative significance of deposits of visceral fat in various racial and ethnic groups. Similar to the present study, Boyko et al. also noted a relationship between body visceral fat and SBP (p=0.004) or DBP (p=0.001).[18]

In this study, body VF is positively correlated with Triglyceride levels (p < 0.001). Additionally, according to Katsuki et al, non-obese Japanese participants with type 2 diabetes showed a positive correlation between VF percentage and Triglyceride levels (p=0.01).[19] In a different study by Kobayashi et al., it was discovered that body visceral fat was significantly correlated with Triglycerides (p=0.01) in Japanese non-obese men.[20] Similar to the current study, Fox et al. found that among 3001 Americans, body VF had a strong positive connection with Triglycerides (p= 0.0001).[11] According to a study by Shweta et al., high levels of visceral body fat in Indian teenagers are positively correlated with blood pressure.[21] Additionally, they concluded that a higher degree of visceral body fat affects the chance of developing cardiovascular diseases. Body visceral fat and High-Density Lipoprotein had a 0.6 association coefficient, which was not statistically significant. HDL was inversely correlated with body fat % in another investigation by Goswami.[22] This contrasts with our study where HDL was positively correlated to VF though not statistically significant. Non-communicable diseases (NCDs) are a major cause of death worldwide today and are a raging epidemic. Therefore, if body VF assessment is included in the amenities of primary healthcare facilities in Pakistan's undeveloped provinces in the future, it will undoubtedly help identify vulnerable populations who are more likely to later develop chronic diseases like CKD, diabetes, and so forth. It may also provide insight on the health of the local populations and their level of understanding regarding the significance of lifestyle choices in the prevention of NCDs.

Conclusion

According to the current study's findings, body VF% was substantially correlated with elevated blood pressure, altered lipid profile, and type 2 diabetes. As a result, standard screening programs at all district-level health facilities nationwide should include body fat percentage analysis.

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Authors Contribution

FI, RKA: Conceptualization of Project
HS, NMB, RKA: Data Collection
AAS: Literature Search
ZAL: Statistical Analysis
FI, RKA, AAS: Drafting, Revision
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Frequency of Reversibility of Complete Heart Block in Acute Myocardial Infarction

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Abstract

Objective: The aim of current study was to determine the frequency of reversibility of complete heart block in patients of acute myocardial infarction.

Method: This was a cross sectional study conducted on 138 patients with complaint of syncope and atypical chest pain presenting at emergency ward of Punjab Institute of Cardiology, Lahore. All patients underwent conventional coronary angiogram to roll out the ischemic etiology of underlying bradyarrhythmias. Among them more than 90% patients have mild coronary artery disease and they were kept on medical management. But all patients remained TPM dependent for two weeks which were then treated with permanent pacemakers. Statistical analysis was performed by using SPSS-20.0.

Results: The mean age of patients was 51.48 ± 15.46 with minimum age 18 and maximum was 65 years. Out of 138 patients, 84(61%) were male while 54(39%) were female. 52(37.7%) patients had diabetes mellitus, 75(54.3%) patients had hypertension and 58(42.03%) patients were smokers. 41(29.7%) had family history, 47(34.1%) patients had dyslipidemia and only 50(36.2%) patients were obese. Only 5(3.6%) hypertensive patients and 4(2.9%) diabetic patients had complete heart block. 2(1.4%) patients presented during 1-12 hours compare with 7(5.1%) presented between 13-24 hours and results showed statistically insignificant as p-value > 0.05. 2nd Degree AV Block and complete heart block showed significant difference between troponin level as p-value <0.05 in patients diagnosed with ACS was significant.

Conclusion: Atrioventricular block is frequently reversible in people with AMI (49%). As a result, in situations with AMI permanent pacemaker installation should be postponed.

Keywords: Atrioventricular Block, Coronary artery disease, Acute Myocardial Infarction, Temporary Pacemaker, Reversibility.

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Introduction

Acute Myocardial infarction (MI) may be complicated with variable degree of heart blocks. These blocks are common with inferior wall MI. In myocardial infarction complicated with heart block,the nature of the block can be determined by the site of myocardial infarction.[1-3] The reversible ischemia to the atrioventricular node produces block in case of diaphragmatic infarction (DMI). It has benign course and is characterized by type I block (Wenckebach) and junctional rhythms. On the other hand, massive septal involvement with necrosis of the bundle branches is seen in anterior infarctions(AMI).[6] Second and third degree blocks and idioventricular rhythms are also common with AMI and have high mortality.[7] In this study, we wanted to determine the frequency of reversibility of complete heart block in patients of acute myocardial infarction.

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Material and Methods

This cross sectional study was conducted on 138 patients

who presented to emergency department in Punjab Institute of cardiology, Lahore-Pakistan with complaint of syncope and atypical chest pain from March, 2020 to June, 2021. Patient of age 18 to 65 years with either gender providing a complete clinical history were included by consective sampling. Patient's age <18 or >65 of both gender and patients those fail to provide complete clinical history were excluded. Informed consent was taken from each patient. From all patients the information regarding demographic parameters was obtained and recorded by entering the data into the proforma designed for this purpose. Family history of IHD, hypertension, diabetes, and smoker was noted very carefully to be used for final data analysis and cross-tabulation to find out the relationship of AMI with miscellaneous factors. The 138 patients underwent conventional coronary angiogram to know the ischemic etiology of underlying bradyarrhythmias. Among them more than 90% patients had mild coronary artery disease and they were kept on medical management. But all patients remained TPM dependent for two weeks which were then treated with permanent pacemakers. Statistical analysis was performed by using SPSS-20.0. The quantitative variables like age and duration of presentation were presented as mean and standard deviation. The qualitative variables like gender, obesity and complete AV block, smoker, hypertension, dyslipidemia, diabetes mellitus and family history were presented as frequency and percentage. Stratification was done for effect modifiers like age, gender, duration of presentation, obesity, smoker, hypertension, dyslipidemia, family history of IHD and diabetes mellitus. Post-stratification Chi square test was applied to see their effects on the outcome and P value ≤ 0.05 was considered as significant.

Results

The mean age of patients was 51.48 ± 15.46 with minimum age 18 and maximum was 65 years. Out of 138 patients, 84(61%) were male while 54(39%) were females. 52(37.7%) patients were diabetic, 75(54.3%) patients had hypertension and 58(42.03%) patients were smoker, 41(29.7%) had family history, 47(34.1%) patients had dyslipidemia and only 50(36.2%) obese patients were registered for the study. (Table 1) . Only 6(4.3%) patients had complete heart block in the age grouped between 16-35 years, as compare with 10(7.2%) in age grouped 36-65 years. Only 8(5.8%) males and 5(3%) females had complete heart block. Only 5(3.6%) hypertensive patients and 4(2.9%) diabetic patients had complete heart block. 2(1.4%) patients presented during 1-12 hours compare with 7(5.1%) who presented between 13-24 hours. Results showed statistically insignificant as p-value > 0.05. (Table-2) 2nd Degree AV Block and complete heart block showed significant difference for reversibility in patients with acute myocardial infarction. (Table-3)

Table 1: *Clinical characteristics of the patients.*

Variables		Frequency
Age	**Mean**	**51.48 ± 5.46 (18-65)**
Gender	Male	84(61%)
	Female	54(39%)
Diabetes	Yes	52(37.7%)
	No	86(62.3%)
Hypertension	Yes	75(54.3%)
	No	63(45.7%)
Smoking	Yes	58(42.0%)
	No	80(58.0%)
Family History	Yes	41 (29.7%)
	No	97 (70.3%)
Dyslipidemia	Yes	47 (34.1%)
	No	91 (65.9)
Obesity	Yes	50(36.2%)
	No	88 (63.8%)

Table 2: *Complete Heart Block and its Association with other Clinical Parameters*

Variables	Complete Heart Block		p-value
	Present	Absent	
Age Group			
16-35	6(4.3%)	44(31.9%)	0.598
36-65	10(7.2%)	78(56.5%)	
Gender			
Male	8(5.8%)	76(55.1%)	0.673
Female	3(2.2%)	51(37.0%)	
Hypertension			
Yes	5(3.6%)	53(38.4%)	0.894
No	8(5.8%)	72(52.2%)	
Diabetes			
Yes	4(2.9%)	71(51.4%)	0.218
No	11(8.0%)	52(37.7%)	
Duration of presentation (h)			
1-12	2(1.4%)	51(37.0%)	0.341
13-24	7(5.1%)	78(56.5%)	

Table 3: *Frequency of Reversibility of Complete Heart Block in Acute Myocardial Infarction*

Characteristics	Present	Absent	p-value
2nd Degree AV Block	15(11%)	4(3%)	0.024
Complete Heart Block	68(49%)	46(33%)	0.040

Discussion

Among 138 patients there were 84(61%) males and 54(39%) females. The frequency of reversibility of complete heart block was 49%. Similar results were found by Fawaz et. al (2014), they enrolled 14 patients, with mean age of 54.3 years (age range was 19-87 years), out of 14 patients 8(57%) were males and 6(43%) were females.[8] In another study by Hajsadeghi et al, the mean age was 34 years with a range between 19 and 55 years.[9] Similarly, in another study conducted by Woodruffet. al, that assessed troponin levels in 49 patients with normal cardiac system, the mean age was 21 years with a range from 15–62 years.[10]

The findings of our study showed that the patients with complete heart block in the age grouped between 16-35 years, only 6(4.3%) as compare with age grouped 36-65 years only 10(7.2%) have complete heart block, male 8(5.8%), only 5(3.6%) hypertensive patients and 4(2.9%) diabetic patients suffering complete heart block, 2(1.4%) patients presented during 1-12 hours compare with 7(5.1%) presented between 13-24 hours, results showed statistically insignificant as p-value > 0.05.

Bhalli et.al, (2009) conducted a study on 345 patients. 303 (87.8%) patients were males and 42(12.2%) were females. 107 (31.01%) had hypertension, 71 (20.5%) diabetes and 119(34.5%) smokers. 153(44.4%) patients had inferior wall MI with arrhythmias as major cause of death.[11]

Another study conducted by Sundhu et. al (2017) found that the mean age was 67 years (95% CI) as compared with other group 75 years (95% CI) with p=0.04. There was no statistically significant difference between the two groups in terms of gender, diabetes, hypertension, or smoking status. 6(12.5%) patients of third degree heart block died as compared to 3 (21.4%) in second group (p=0.327).[12]

Similar study was conducted by Yildiz et al, who concluded that four patients presented with second or third degree AV block were not having acute myocardial infarction and vasovagal syncope.[13]

Meineet al[14] concluded that the incidence of complete heart block was 3.2% overall which is 2 –4% less than in studies of patients with ACS.[14] Nguyen et.al. had similar results as ours. However, patients had NSTEMI who were not at the same risk of heart block. [15]

The main limitation of our study was that it was a single centered study.

Conclusion

Atrioventricular third degree block is frequently reversible in people with AMI (49%). As a result, in situations with AMI permanent pacemaker installation should be postponed. we suggest that, protocols should be designed in our routine clinical practice to deal with such a life threatening condition.

Conflict of Interest: *None*

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Authors Contribution

SM: Conceptualization of Project
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SUM: Writing of Manuscript

Comparison of Characteristics of Methotrexate Tolerant and Intolerant Patients Having Rheumatoid Arthritis

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Abstract

Objectives: To compare the characteristics of methotrexate-tolerant and intolerant patients having rheumatoid arthritis. To determine the association of methotrexate intolerance with the patient and disease-related factors.

Method: This cross-sectional study was carried out at the rheumatology department of Combined Military Hospital Lahore from 31st April to 30th June 2022. It included 181 rheumatoid arthritis (RA) patients using methotrexate (MTX) for > 3 months. Patient demographic variables, disease duration and activity, and information regarding MTX intake were recorded. English methotrexate intolerance severity score (MISS) questionnaire was used to calculate MTX intolerance. Different variables were compared between methotrexate-tolerant and intolerant patients. Association of age, disease duration, and activity, MTX route/dose with MTX intolerance was determined.

Results: The majority of patients were females 140(77%). The median disease duration was 6(1-40) years. MTX intolerance was found in 48(26.5%) of RA patients. Intolerant patients had a higher disease activity score (DAS 28>5.1 in 20.8 vs 3.8%; P = 0.002) and longer duration of MTX intake in months (23.5 vs 12; p=0.018) compared to tolerant patients. Additionally, MTX intolerance was associated with younger age, longer disease duration and higher MTX dose>10mg/wk (P=0.007, P=0.025, P=0.050). There was no significant difference between the two groups in gender, marital status, education, and use of other DMARDs or steroids. (P >0.05).

Conclusion: There was a significant association between age, disease duration, and MTX dose with MTX intolerance. We also noted a significant association between disease activity and route of intake with MTX intolerance but this was lost when adjusted for multiple confounders.

Keywords: methotrexate, intolerance, rheumatoid arthritis, arthritis

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Introduction

Rheumatoid arthritis (RA) is the most frequent deforming inflammatory arthritis, affecting 24.5 million people worldwide and imposing a huge personal and socioeconomic burden.[1] Methotrexate (MTX) is the most commonly used disease-modifying antirheumatic drug (DMARD) for the treatment of RA as it has excellent efficacy and very low toxicity.[2] MTX relieves pain, maintains normal muscle strength, and preserves joint function while preventing growth retardation and joint deformities. It has been used as the first-line treatment of inflammatory arthritis for more than two decades.[3]

However, many patients are shifted to an alternative and more expensive DMARD when they do not tolerate MTX. MTX intolerance is found in 30%-60% of patients.[4] It produces a combination of symptoms, including nausea, vomiting, abdominal pain, and irritability. It is essential to ask about these symptoms because a significant pro-

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portion of patients discontinue treatment and suffer from decreased quality of life while using MTX.[5] These symptoms not only occur after taking it but also before taking it, and even upon thinking about it.[6] In addition adult patients may also experience fatigue, headache, dizziness, irritation, diarrhea, and hair loss.[7]

Almost half of the patients discontinue MTX with or without informing their physician within six months to two years.[8] Different factors like age, gender, marital status, pain, and disease activity affect MTX intolerance. The behavioral component is very important as MTX-intolerant patients have more patient-reported outcomes.[9] MTX intolerance is also related to the route of intake.[10] That is the reason why managing intolerance includes patient education, counselling, and changes in dose and route of medication.[11]

MTX is the foundation of the management of RA, and it should be continued in all patients unless any contraindication arises. Intolerance of this drug is common, yet various factors affecting it are usually ignored. It is of utmost importance to be aware of the differences between MTX-tolerant and intolerant patients so that such individuals can be monitored closely for possible early intervention to ensure adherence to this vital therapy. Previously this issue has not been assessed. Therefore, the primary objective of this study was to compare the characteristics of MTX-tolerant and intolerant patients with RA and to establish the association of MTX intolerance with patients and disease-related factors.

Materials and Methods

We enrolled 181 patients with RA classified according to ACR/EULAR 2010 classification,[12] who had been on regular MTX for more than three months and were regularly followed up in the rheumatology outpatient department. We calculated the sample size by taking the frequency of MTX intolerance as 21.6%, CI as 95%, and margin of error as 6%.[13] Our RA patients were between eighteen and sixty years. Those patients who were non-compliant (who had discontinued more than two medicines in the past without a reason) or those with cognitive impairments, a history of peptic ulcer disease, or gastrointestinal (GI) complaints before going on MTX were excluded. We recruited our patients using convenience sampling after obtaining informed written consent. We interviewed these patients to assess intolerance. To avoid any bias, a single person asked the same set of questions, and patients were blinded to the results of their questionnaires. We recorded demographic details, comorbidities, and pain VAS (pain described by the patient with the help of a 100mm visual analog scale). We noted disease duration and activity, the serology status of the patients, and the dose/duration and route of MTX. We calculated intolerance to MTX using the MISS questionnaire after obtaining permission from the research team of the University Medical Center, Utrecht, Netherlands. This questionnaire comprises four areas: abdominal pain, nausea, vomiting, and behavioral issues. A patient score of six points or higher, inclusive of at least one anticipatory, associative, or behavioral symptom, is labeled as MTX intolerant.[14] MTX dose was prescribed by the rheumatologist. The treating rheumatologist reviewed and monitored the patients for any drug side effects. We entered data using IBM SPSS Version 26. Quantitative variables like age, disease duration, MTX dose and duration, and pain VAS were presented as means with standard deviation or median with interquartile range (IQR). Qualitative variables like gender and route of MTX were presented as frequency and percentages. For the normally distributed data, we used the t-test, and for abnormally distributed data we used the Mann- Whitney U test to compare the MTX-tolerant and intolerant patients. We used a chi-square test to compare the categorical variables between the two categories. After adjusting for confounding variables, we applied bivariate logistic regression to determine factors related to MTX intolerance. $P<0.05$ was regarded as statistically significant.

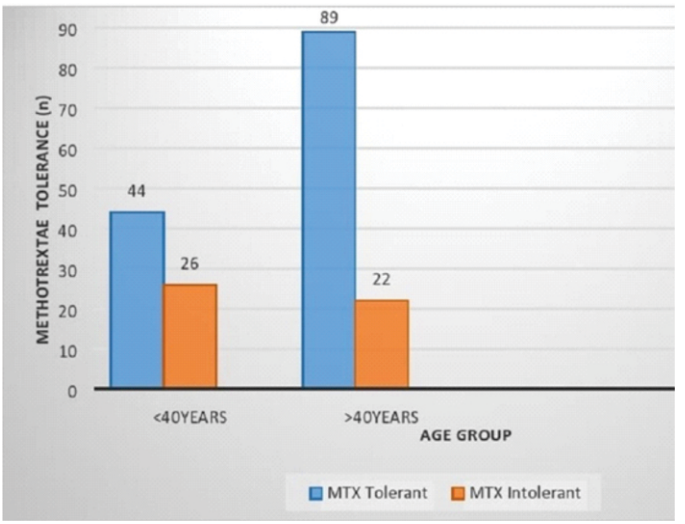
Results

We included 181 RA patients. The MTX was given by oral route in 159 (87.8%) patients and the other 22 (12.2 %) got it subcutaneously (SQ). MTX intolerant patients had a higher pain VAS (50 vs. 20; p=0.50), a higher DAS 28 value (p=0.002), and a long history of MTX intake (23.5 vs. 12 months; p=0.018) compared to tolerant patients. MTX intolerance occurred more often in patients receiving MTX by injectable route than those taking it by mouth (50% vs. 28%). (Table 1). IQR-Interquartile range; SD-Standard deviation; DAS-Disease activity score; VAS-Visual analog scale; MTX-Methotrexate; DMARD-disease-modifying anti-rheumatic drug MTX intolerance was identified in 48 (26.5%) of the patients. Nausea was the predominant symptom occurring in 45(93.8%) followed by restlessness in 38 (79%) and irritability in 37(77%) of the MTX-intolerant patients. MTX intolerance was associated with younger age (adjusted odds ratio (AOR 3.152; 95% CI 1.360, 7.307, P = 0.007), longer disease duration (AOR .341;

95% CI .133,.871, P = 0.025) and higher MTX dose> 10mg/wk (AOR .418; CI .175-.998, P= .050). We also found a significant association between SQ route, and disease activity (pain VAS, DAS 28) with MTX intolerance, but after applying logistic regression the p-value was not significant. MTX intolerance increased with disease duration, as 39/48 (81.3%) patients who were intolerant had a disease of more than three years (p= 0.025). Those who were taking more than 10mg/week of MTX showed more intolerance (p=0.05).
Comorbidities were found in 32(17.7%). There was no relation between MTX intolerance to gender, marital status, smoking history, or education level. (Table 2) MTX-Methotrexate; DAS 28-Disease activity score 28; VAS-Visual analog scale. Younger age was associated with more intolerance to MTX (p=0.007). Of the forty-eight MTX-intolerant patients, only ten (20.8%) were over fifty years (p=0.007; FIG 1). MTX intolerance was associated with disease activity as measured by DAS 28. Most of the patients having low disease activity were tolerant 77/92 (84%) while most patients having high disease activity 10/15 (67%) were intolerant.

Table 2: *Factors Associated with MTX Intolerance-Bivariate Logistic Regression*

Factors	Adjusted Odds Ratio	95% Confidence Interval	p-value
Gender	1.602	0.574-4.47	0.368
Age(years)	3.152	1.360-7.307	**0.007**
Marital status	1.055	0.290-3.832	0.935
Education	0.532	0.237-1.194	0.126
Disease duration	0.341	0.133-0.871	**0.025**
MTX duration	0.970	0.424-2.220	0.943
MTX dose	0.418	0.175-0.998	**0.050**
MTX Route	0.458	0.148-1.413	0.174
Pain VAS	0.376	0.136-1.037	0.059
DAS 28	0.622	0.242-1.602	0.326



MTX-Methotrexate

Fig-1. *Comparison of Age with Methotrexate Tolerance*

Discussion

MTX is the standard of care in RA patients in doses of less than 25-30mg/week. Low-dose (LD) MTX received FDA approval in 1988 for its use in RA as an anti-inflammatory drug with fewer adverse effects and almost no toxicity compared to high-dose (HD) MTX used in malignancies, where it acts as an anti-proliferative cyto-

Table 1: *Baseline Characteristics and Comparison of Variables Between Methotrexate-Tolerant and Intolerant Patients*

Variable	All (n=181)	MTX-Tolerant (n=133)	MTX-Intolerant (n=48)	p-value Tolerant vs Intolerant
Female n(%)	140 (77%)	99 (74%)	41 (85.4%)	0.119
Male n(%)	41 (23%)	34 (25.6%)	7 (14.6%)	0.119
Age [Mean (SD)]	43.3+11.9	45.02+11.72	38+11.43	0.861
Duration of disease (years) Median (IQR)	6 (7)	6 (9)	6 (5.5)	0.56
Dose of MTX (mg/week) Median (IQR)	15 (10)	15 (10)	10 (5)	0.879
Duration on MTX (months) Median (IQR)	12 (34)	12 (30)	23.5 (42)	0.018
Injectable MTX n(%)	22 (12%)	11 (8.3%)	11 (23%)	0.008
DAS 28 (>5.1)	15 (8.3%)	5 (3.8%)	10 (20.8%)	0.002
Pain VAS Median (IQR)	30 (30)	20 (35)	50 (40)	0.50
Use of folic acid n(%)	173 (95%)	126 (94.7%)	47 (97.9%)	0.358
Use of other DMARDS n(%)	76 (42%)	57 (42.9%)	23 (47.9%)	0.139
Using steroid n(%)	84 (46%)	60 (45%)	24 (50%)	0.561

toxic drug associated with more toxicity.[15] At low doses RA patients showed significant response compared to placebo both clinically and statistically as measured by ACR 5O response at three months and one year.[16] MTX intolerance was found in 26.5% of our patients, with nausea and behavioral symptoms being the most frequent. In a study done on 117 RA patients, 55 (47%), patients reported MTX intolerance with predominantly behavioral symptoms.[9] Haya et al. observed various side effects with MTX in 33% of patients, with GI symptoms being the most common (53%), especially in younger patients.[17] We found that MTX intolerance decreased with age, as most patients above fifty were tolerant to MTX. Braun et al. similarly reported less intolerance in patients over sixty-five.[18] The ideal route for MTX therapy in RA is not yet confirmed. The safety, efficacy, and tolerability of oral and parenteral MTX are comparable. Hence oral is always the preferred starting therapy.[18-19] In contrast, Li D found that the SQ of MTX had better bioavailability and clinical efficacy at higher doses, reducing nausea and diarrhea, but the treatment failure rates were comparable with those of the oral route.20 Another study documented higher MTX intolerance on parenteral (67.5% vs. 44.5%) compared to the oral route (p=0.001).[21] The oral route is almost always preferred by both patient and physician, and most patients in our study who were on SQ MTX were primarily started on oral and were later shifted to SQ by the treating physician due to intolerance, which persisted in 50% of them despite shifting mainly because of the behavioral component.

We found a strong association of MTX intolerance with DAS 28 but no influence of gender, marital status, or education, while Amalog found a strong association of MTX intolerance not only with pain VAS (p=0.010) and DAS 28 (p=0.036) but also with female gender (p=0.016) and marital status (p=0.042).[9] Kaya et al. studied MTX in all age groups and found different risk factors associated with MTX intolerance, including younger age, patient VAS scores, and parenteral route of administration ($p<0.05$).[22] We noticed that patients taking more than 10mg/week of MTX were more intolerant, but the use of other DMARDs did not affect tolerance. However, apart from a younger age, Mahroug et al did not find any effect of dose, duration, route of MTX administration, or other DMARDs on tolerance (p=0.048).[23-24] In our study, we noticed that MTX intolerance was more common in patients who had RA for more than three years and were taking MTX for longer. It is known that MTX-induced nausea is inversely related to age, but we still do not know which factors affect MTX's metabolism and effects. As intolerance is more common in patients using MTX for more than one year, there might be a cumulative effect of MTX on nausea.[25] Limitations of our study include a small sample size and it included only one ethnic group. Moreover, the number of patients using SQ MTX was much less than the ones using oral MTX. We recommend future studies including a larger sample size on possible ways to increase adherence to MTX therapy. The use of a smartphone for the digital monitoring of remote patients could be an option.

Conclusions

MTX intolerance is common among the Pakistani RA population and is related to younger age, higher doses of MTX, and longer disease duration. We need to educate patients about the benefits of taking MTX, which will improve the behavioral factors related to its use and address at an earlier time any untoward symptoms related to intake, thereby increasing compliance with the medication.

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Authors Contribution

SS, RK: Conceptualization of Project
BA: Data Collection
SS, SK, RK, BA: Literature Search
SS, RK, BA : Statistical Analysis
SS, SK, RK, BA: Drafting, Revision
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Association of Serum Cortisol Levels with Respiratory Distress Syndrome and Mortality in Premature Babies

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Abstract

Objective: To determine the association of serum cortisol levels with Respiratory distress syndrome and Mortality in premature babies

Method: A descriptive cross sectional study was conducted in Neonatal unit of pediatric medicine 1 of BahawalVictoria hospital Bahawalpur from Feb 2021 to June 2021.Premature babies (less than 36 weeks gestation by ballard scoring) admitted in Preterm ward on day 1 were enrolled after informed consent and ruling out exclusion criteria (More than 24 hour old , Who have received antenatal steroids for lung maturation, Received any treatment before admission in any other hospital, Patient having Any obvious anomaly). Day 1 sample sent for CRP and cortisol. Data recorded regarding weight, gestational age (ballard scoring), septic risk factors. These patients were followed for development of RDS (on X ray at 24 hour of life). Outcome was documented as expiry, discharged or LAMA. Data analyzed in SPSS 20.

Results: 40 patients were enrolled as per inclusion criteria. 27 (67.5 %) were male and 13 (32.5 %) were female. Gestational age 3 (7.5 %) had less than 28 weeks, 29-30 weeks were 6 (15 %), 31-34 weeks were 31 (77.5 %). Weight less than 1.5 kg were 23 (57.5%), 1.5 to2 kg were 15 (37.5 %), 2.1-2.5 kg were 2 (5%). Cortisol level low in 4 (10 %), normal in 6 (15 %), high in 30 (75 %).22 (55 %) discharged, 13 (32 %) expired, and 5 (12.5 %) got LAMA. Cortisol level as compared to outcome has p value 0.002. Tweleve (30 %) had RDS. Twenty two (55 %) had clinical evidence of sepsis. 18 (45 %) had CRP more than 6. Cortisol level as compared to RDS presence has P value 0.057 and with sepsis has P value 0.007. Mean cortisol in discharged patients were 19.8, expired 14.2 and LAMA has 22.7. Mean cortisol level in RDS patients were 18.3 and RDS absent had 18.3 also. Mean cortisol level in Sepsis positive patients were 18.6 and sepsis absent were 18.0

Conclusion: Mean cortisol has no significant difference in discharged and expired patients.

Keywords: Cortisol, Respiratory distress syndrome(RDS), Mortality, Premature Babies

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Introduction

Pakistan is among the top ten countries where two third premature babies dies every year. An estimated 860,000 babies are born preterm every year and among those almost 11.8 die % due to complications of pre-maturity.[1] Preterm infants have to face lot of compli-cations after birth, respiratory distress syndrome, necro-tizing enterocolitis, weekend immune system, retino-pathy of prematurity, chronic lung disease, and neuro-logical insult etc.[2] As prematurity is the most common cause of infant mortality, the respiratory distress synd-rome is the leading cause of mortality in premature infants.[3] It is an alarming situation and every effort should be made to decrease the morbidity and mortality of preterm infants.

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During fetal life adrenals start secreting cortisol at almost 8 weeks of gestation but it is not the main steroid. Dehydroepiandrosterone (DHEA) and its sulphates (DHEAS) are the main steroids during fetal life and act as substrate for placental estrogen production.[4] Normal development and functioning of adrenal glands is essential not only for fetus but also for neonatal life thereafter. For example, fetal miss programming of the stress axis not only alter fetal cortisol production but may predispose to diseases in later life. If the hypothalamic adrenal axis is not properly activated, it may result in physiological instability which in turn adversely affects the severity of illness, morbidity and mortality.[5] The preterm newborns are more prone to develop relative adrenal insufficiency because they have limited 3 β-hydroxysteriod dehydrogenase (HSD) and the other enzymes for the synthesis of cortisol. 3 β-HSD is expressed from adrenal neocortex after 23 week of gestation, before that fetus uses progesterone from placenta to produce cortisol.[6] Antenatal steroids have shown some beneficial effects in prevention of respiratory distress syndrome.[7] As it is stated above the preterm babies have low cortisol levels and also have relative adrenal insufficiency. If it is proved that the premature babies with low serum cortisol levels have increase morbidity due to RDS and increase mortality, the post natal steroid therapy can help in decreasing the morbidity and mortality of premature babies.

The prophylactic use of steroid in prematures have been a controversy because some trials have suggested that it prophylactic use increase the survival of extreme preterm without broncho pulmonary dysplasia, but on the other hands the steiods have some unaccepted risks like intestinal rupture in prematures.[8]

The rationale of this study is that if we are able to prove that the low serum cotisol levels have association with prevalence and severity of RDS and with mortality of prematues, then we can suggest the prophylactic use of steroids in prematues that will improve their outcome. Although surfactant therapy has definitive role in treatment of RDS, but due to limited resources it is not available in every health care facility dealing with prematures, but steroids are easily available, cheap and if it plays role in prevention of RDS that it will also help in reducing disease burden. Premature babies (less than 36 weeks gestation by ballard scoring admitted in neonatal unit of pediatric department on first day of life. Preterm babies who have received antenatal steroids for lung maturation,

- History of delayed cry or resuscitation required at birth
- Patients having any obvious anomaly
- Patients who received any treatment before admission in any other hospital

Materials and Methods

It was a descriptive, Cross Sectional Study conducted in Department of Pediatrics, Bahawal Victoria hospital, Bahawalpur, from Feb 2021 to June 2021. Total forty premature babies admitted in pediatric department who met the inclusion and exclusion criteria were included in the studies after taking informed consent. Gestational age was determined by using expanded Ballard score. Non-probability consecutive sampling technique was used. After inclusion, patient's demographic, social, personal data, status of respiratory distress syndrome and septic profile was entered on pre-designed proforma. On first day of life (early morning) blood sample were sent for serum cortisol and CRP. Sepsis was labeled on the basis of clinical presentation and raised CRP. All the labs reports were entered on proforma and finally the fate of the patient was also entered.

The data was entered and analyzed by using SPSS version 20. Mean and Median was calculated for numerical data. Frequency, percentages and p-value calculated for serum cortisol, sepsis, RDS status and mortality.

Results

Forty patients were enrolled as per inclusion criteria. 27 (67.5 %) were male and 13 (32.5 %) were female. Three (7.5 %) patients had gestational age less than 28 weeks, 6 (15 %)were of 29-30 weeks gestation, 31-34 weeks were 31 (77.5 %). Patients having weight less than 1.5 kg were 23 (57.5%), 1.5 to2 kg were 15 (37.5 %), and 2.1-2.5 kg were 2 (5%). Serum cortisol levels ranges from 1.1 to 46 IU with mean value of 18.36 IU. Cortisol level were low in 10% of preterm infants, 15% were having normal cortisol levels while it was high in 30 (75 %) of preterm babies. Regarding outcome twenty-two (55 %) discharged, 13 (32 %) expired, and 5 (12.5 %) got LAMA. Cortisol level as compared to outcome has p value 0.002(Table 1). Twelve (30 %) had RDS. Twenty-two (55 %) had clinical evidence of sepsis. 18 (45 %) had CRP more than 6. Cortisol level as compared to RDS presence has P value 0.06 (Table 2) and with sepsis has P value 0.007. Mean cortisol in discharged patients were 19.8, expired 14.2 and LAMA has 22.7. Mean cortisol in RDS patients were 18.3 and RDS absent had

18.3 also. Mean cortisol in Sepsis positive patients were 18.6 and sepsis absent were 18.

Discussion

In our study 77.5% preterm babies were between 31-34 week gestation and 75% of our preterm babies were having high cortisol level. While in many of the other studies the premature babies were having serum cortisol levels within the reference range for their gestation[9,10]. However the serum cortisol levels were inversely proportional to the gestational age in our study, similarly Seshagiri, et al concluded in their study that the serum cortisol levels were declined with increasing gestational age in healthy term and preterm babies[11]. Some studies have concluded that the serum cortisol levels were high in small for gestational age babies as compared to appropriate for gestational age.[9] We had included only appropriate for gestational age preterm babies in our study, so we can't comment on serum cortisol levels in small for gestational age babies. Respiratory distress syndrome (RDS) was diagnosed in 30% of our preterm babies included in study. While comparing the serum cortisol levels of those with RDS and without RDS, there was no statistically significant difference in both groups. It means serum cortisol level does not play any significant role in development of RDS in preterm babies. Reynolds JW concluded in his study that adrenal hypo function does not play any role in development of RDS in premature babies.[12] While in 2020 a study conducted in Egypt concluded that that serum cortisol levels has positive correlation with respiratory distress syndrome in preterm babies[13] that is contrary to our study results. They have large sample size than ours, so more research and data is needed in future. Similarly results were concluded by a study conducted in turkey.[14] Beverley E. Person Murphy conducted a research in Canada in 2015, in which he said the both the cortisol and cortisone levels were low in cord blood of babies who developed RDS.[15] Elevated serum cortisol has significant effect on pediatric mortality in pediatric intensive care unit (PICU) described by Osama E. Bekhit and colleges in 2015.[16] While talking about effect of serum cortisol and adrenal insufficiency on preterm mortality, Sari F.N concluded that there is no correlation between serum cortisol and mortality in preterm infants.[17] But in our study low serum cortisol levels has significant effect on mortality. In October 2007 a study conducted in Kuopio University Hospital, in this study they have taken cord blood, and serum cortisol and DHEAS concentrations on day one and four of life. It was seen that the low serum cortisol and DHEAS levels in cord blood and first day of life has significant effect on outcome.[18]

Table 1: *Outcome in relation to serum Cortisol levels*

Cortisol Groups	Number of patients	Discharged	Died	LAMA
Low (0-2)	4	4	0	0
Normal (2-11)	6	0	6	0
High (12-100)	30	18	7	5
P Value = 0.002				

Table 2: *RDS status in relation to Serum Cortisol Levels*

Cortisol Groups	Number of patients	RDS Present	RDS Absent
Low (0-2)	4	0	4
Normal (2-11)	6	4	2
High (12-100)	30	8	22
P Value = 0.06			

Conclusion

Serum cortisol was high in 75% of my study population. Low cortisol has good outcome as compared to those having high cortisol level. Cortisol level has no significant relation to the presence of RDS.

Conflict of Interest: *None*

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Authors Contribution

MS: Conceptualization of Project
MN: Data Collection
NF: Literature Search
MS: Statistical Analysis
NF: Drafting, Revision
MS: Writing of Manuscript

A Cohort Analysis Between Artificially Sweetened Beverages' Consumption And Weight Gain Risk Among Uk Children: A Prospective Study

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Abstract

Objective: The modern lifestyle raises serious concerns about the quality and variety of food available, and it has been suggested that increased intake of sweetened and artificially sweetened beverages may be a contributing cause to obesity. The goal of this study was to look into the contentious claim that children in the UK who consume artificially sweetened drinks (ASB) had higher risk of overweight and obesity.

Method: Data were gathered from the Millennium Cohort Study (MCS), and secondary analysis was carried out, including bivariate analysis on 12,871 kids and multinomial regression for obesity on 8,838 kids. The consumption of ASBs was recorded as exposure, and overweight or obesity was chosen as the outcome variable. Children who were already overweight or obese at the beginning of data collection were not included in the regression analysis. This group of children was followed up prospectively for 5 years, ending with the MCS wave.

Results: Children who consumed ASB more than once a day had a 39% greater risk of being overweight compared to non-consumers (RRR=1.45; CI: 1.16-1.80), and an almost 4 times higher risk of being obese compared to children who did not drink ASB more than once per day (RRR=3.96; CI: 1.50-10.47).

Conclusion: This study concluded that there is significant relationship in ASB consumption and risk of getting overweight/obese when observed prospectively.

Keywords: Artificially Sweetened Beverages, Artificial Sweeteners, Childhood Obesity, Millennium Cohort Study.

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Introduction

Childhood obesity is titled as world-wide epidemic or pandemic and fosters an ever-expanding concern among public health professionals and health policy makers.[1] The phenomenon of increase in childhood obesity is observed not only among developed countries but also among developing countries[2,3] and this leads to enthralling emphasis on research in this domain. An extensive epidemiological study on obesity in children and young people estimated that approximately 10% of the school-aged children to be overweight or obese world-wide. Around the globe, 170 million children were considered to be classified either overweight or obese.[4] Large nationally representative surveys indicated high prevalence of obesity was found, as low as 11% and as high as 34%, in European countries.[5] Epidemiological evidence of Sugar sweetened beverages (SSB) related with the risk of obesity is well established. Obesity and related chronic diseases had shown an upsurge in prevalence globally.[6,7] Simultaneously, temporal patterns in increased global use of SSB showed a close

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parallel with these diseases.[8] However, the simultaneous rise in consumption of artificially sweetened beverages is also reported making their controversial role in obesity more questionable.[9] Artificial sugars were extensively consumed by diabetic patients and healthy individuals on doctors' and dietitians' recommended sugar restricted diets. Pharmacological names of commonly used artificial sweeteners are Saccharin, Cyclamate, Aspartame, Neotame and Sucralose etc. These compounds belong to multiple groups or categories of nutrition supplements with variety of routes of metabolization.[10] Pharmacologically, these artificial sweeteners do not have good safety profile as well.[11] Considering their involvement in risk of obesity, artificial sweeteners and weight gain are well connected[10,12,13] as evident by studies on albino rats and review articles. However, the longitudinal effect of artificial sweeteners on weight gain among human is not well established. These artificial sweeteners are added in beverages with the aim of furnishing the appetency of sweetness but not adding up the calories. However, their role in health stands controversial as large cross-sectional and longitudinal studies done on children have proclaimed positive association between their consumption and obesity but on the contrary, small scale Randomized Trials with insufficient strength, have found little association between ASB consumption and weight gain.[14] Current scientific literature is found deficient to provide consistent evidence about the association between ASBs and obesity. Most of the observational studies are show clear associations between ASB consumption and obesity. But observational studies are considered to be weaker in the hierarchy of evidence. On the other hand, most RCTs did not find causal role of ASBs in the development of obesity. Similarly, systematic reviews and meta-analysis provided mixed results because of researches with conflicted outcomes. This study was carried out with the aim of evaluating the evidence between ASB consumption and obesity among children, using cohort study design.

Material and Methods

The Millennium Cohort Study (MCS) was carried out as prospective cohort study of UK children. This study was essentially Prospective Cohort in its nature as the children were first assessed on baseline and then they were followed up after five years. This study followed multiple life aspects of over 13,000 children with the consent of parents of the children. Ethical clearance from Research Ethical Committee (REC) was acquired for collection of data of main surveys[15] and it was obtained from University of London. The data was available in anonymized state and freely available for academic use, which doesn't need any copy-write approval[22]. The data was obtained from MCS and secondary analysis was done using STATA 12.0. Data collection was done using face-to-face interviews, house-hold questionnaires, cognitive assessments and physical measurements taken by experts. Overweight/Obesity was selected as outcome variable. This variable was derived from Body Mass Index (BMI) which was calculated from cohort members' weights and heights. The apparatus used to measure Height was Leicester Stadiometer and the appliance used to measure weight and body fat percentage was Tanita BF-522W. Children's BMI is classified as overweight or obese utilizing thresholds that change according to child's age and sex. The thresholds are deduced from a reference population called Child Growth Reference. It consisted of 3 categories: Healthy weight, Over-weight and Obese. These categories were graded using BMI which was calculated from cohort members' weights and heights. Exposure of ASBs' consumption was recorded and categorized into 7 categories. This measure encompasses the frequency of sugary drink consumption in cohort members as reported by the main respondent and confirmed by parents. Following covariates were included in the analysis: Gender, Ethnicity, Equalized Income Quantiles, Mothers' education level, Physical activity of cohort member. Income data was collected through information on multiple measures of main carer's and partner's total take-home income and savings. Some of these measures were gross earning, net earnings, earning from second job or occasional work, housing benefits, net benefits, state pensions, income support, working tax credits etc. Modified OECD scales were applied to equivalise the family income. Modified OECD scales adjust take-home income according to family size (1 parent and one child under 14). This variable has been categorized into 5 quintiles of equivalized family income.

Bivariate analysis was carried out between the outcome and exposure and multiple covariates to assess the crude association. This analysis was executed to find out the prevalence of overweight and obesity among different categories of variables without adjustment. Chi square test was used for test of significance in bivariate analysis. To over-rule under-representation bias and over-representation bias in sampling methods, survey weights were administered before running this analysis.[16] Reg-

ression analysis was done to evaluate the effects of beverage consumption for children who had been a healthy weight at early childhood and start of MCS sweep. This analysis excluded the children who were already overweight or obese at the start of data collection. This subsample of children was observed prospectively over the period of 5 years and by the end of wave of MCS, observations were taken again. P-value of less than 0.05 was set for significance level testing.

Results

The prevalence of obesity among different categories of exposure variables and covariates are shown in Table 1. Bivariate analysis was conducted on 12,871 partici-pants using survey weights to account for the complex sampling design. Bivariate analysis showed that girls were significantly more likely to be overweight or obese than boys. ASB consumption showed a strong association with obesity. The prevalence of overweight and obese grew considerably as frequency of ASB consumption increased. Chi-squared test showed significant trend in obesity associated with ASB. Mothers' education appeared to be a significant protective factor against obesity. Analysis showed that on average, obesity was less prevalent in the higher the mother's education level. Socio-economic factors (ethnicity, equivalised income quintiles and parental social class) were significantly associated with obesity in bivariate analysis. Physical activity was also significantly associated with obesity. Children frequently involved in physical activity were less likely to be overweight and obese. Among children involved in 5 or more days of physical activity only 3.18% were obese, while obesity percentage among physically inactive children was 8.36%.

Table 2 presents multi-nominal regression analysis of children who were not overweight or obese at the age of 7. This analysis was carried out to reduce the possibility of reverse causation, as it might be that parents bought artificially sweetened drinks for children who were already overweight to reduce their sugar intake. After removing overweight and obese children in the sample, 8,838 children were included in this analysis.

Table presents the fully adjusted multinomial regression models. The Relative Risk Ratio (RRR) of being overweight or obese increased with increased exposure to ASB consumption frequency. ASB consumption was associated with an increased relative risk of being overweight and obese also among the children with healthy weight. Children consuming ASB more than once a day

Table 1: *Bivariate Analysis between Covariates and overweight/ obesity and BMI; Total Observations (N): 12,871*

Variables	Categories	Overweight/Obesity		
		Overweight n (Weighted %)	Obese n (Weighted %)	P-Value
Child's Gender	Male	1,273 (19.18)	417 (6.22)	<0.001
	Female	1,444 (22.91)	443 (6.65)	
Child's Age	10 Years	936 (21.57)	293 (6.77)	0.136
	11 Years	1,764 (20.61)	561 (6.25)	
	12 Years	17 (31.12)	6 (6.02)	
ASB Consumption	Never	466 (17.63)	117 (4.21)	<0.001
	1-2 days/week	417 (22.01)	119 (6.73)	
	3-6 days/week	243 (22.78)	80 (6.68)	
	Once a day	449 (21.85)	173 (7.59)	
	>Once a day	606 (23.44)	241 (8.84)	
	Missing	127 (21.53)	42 (6.06)	
Mother's Education	Post Grad Level	184 (18.09)	42 (3.15)	<0.001
	Degree Level	639 (17.95)	163 (3.97)	
	A Levels	241 (22.11)	57 (4.60)	
	GCSE Grade A-C	879 (22.95)	267 (6.60)	
	GCSE Grade D-E	265 (21.25)	112 (9.71)	
	Missing	12 (23.52)	6 (14.57)	
Child Ethnicity	White	2,194 (20.43)	669 (5.93)	<0.001
	Mixed	8 (23.66)	31 (9.79)	
	Asian	283 (23.53)	98 (6.59)	
	Black	117 (27.14)	52 (13.22)	
	Other Ethnic groups	40 (19.07)	9 (4.18)	
	Missing	0 (0)	1 (27.77)	
Equivalised IncomeQuintiles	Top Quintile	403 (17.84)	74 (3.09)	
	2nd Quintile	519 (20.56)	116 (4.23)	
	3rd Quintile	601 (22.62)	179 (6.48)	<0.001
	4th Quintile	585 (22.58)	252 (9.33)	
	Bottom Quintile	609 (20.99)	239 (8.25)	
Parental Social Class (Current Job)	Managerial & Professional	639 (19.88)	162 (4.23)	
	Intermediate	385 (19.24)	98 (4.96)	
	Small employer	175 (22.08)	54 (7.37)	
	Low Supervisory & Technical	60 (23.78)	23 (7.15)	<0.001
	Semi-routine & routine	546 (22.29)	149 (6.79)	
	Missing	1,002 (21.45)	374 (8.00)	
Frequency of Physical Activity	5 or more days/week	178 (17.20)	36 (3.18)	<0.001
	4 days/week	184 (17.37)	42 (4.09)	
	3 days/week	368 (18.91)	98 (4.61)	
	2 days/week	507 (18.98)	160 (6.25)	

had a 45% increased risk of being overweight (RRR= 1.45; CI: 1.16-1.80), and an almost 4 times higher risk of being obese compared to non- consumers (RRR= 3.96; CI: 1.50-10.47).

Discussion

The associations between ASB and overweight/ obesity were robust when tested in multi-nominal analysis which included only children who were not overweight or obese at the beginning of the study. The aim of this analysis was to see the impact of beverage consumption in healthy weight children in an attempt to rule out the possibility of reverse causation. The analysis showed that healthy weight children who consumed ASB more than once a day were approximately 50% more at risk of being overweight. The risk of being obese under exposure of frequent ASB consumption was 4 times higher than no ASB consumption. The plausible explanation behind weight gain in response to ASB consumption may be given by research studies revealing that childhood weight gain is attributed to developmental programming of metabolism and metabolic hormone secretion by direct or indirect exposure to artificial sweeteners[17]. However, more research is needed to fully understand the effects of artificially sweetened beverages on weight gain risk. The findings of reviews on link between artificial sweeteners and obesity also confirm that artificial sweeteners utilization leads to metabolic syndrome and obesity[18]. Study on metabolic effects of diet cola consumption in blood showed a similar rise in the blood glycemic levels as with consumption of glucose consumption and sweetened beverage consumption[19]. Another explanation behind the results of our study is that this weight gain may be due to a phenomenon called "compensation," where individuals who consume these types of beverages may feel they have "saved" calories and then overcompensate by consuming more calories later on. Additionally, some research suggests that artificial sweeteners may disrupt the body's natural ability to regulate calorie intake, leading to weight gain[21]. However, contrary to other studies, one study also reported contrasting results of showing no long term effects of aspartame consumption on glycaemia and appetite[20]. However, small sample size and study duration and not including regression analysis to neutralize the effects of confounding factors were the weaknesses of above mentioned study. This study's strengths included a large sample size of UK children and analyzing the impacts ASB consumption on a longitudinal and prospective pattern and use of multi-nominal regression modelling technique. In summary, our study provided a substantial evidence of effects of ASB consumption on risk of getting obese among the UK children.

Table 2: *Subsample Analysis Multinomial Regression for Obesity after Adjusting for all Variables. Observations N: 8,838*

Categories	ASB ConsumptionRRR (95% CI)	P-Value
Not Overweight+ Underweight		
Ref RRR: 1		
Overweight		
Never	Ref RRR: 1	
1-2 days/week	1.21 (0.65-1.54)	>0.05
3-6 days/week	1.33 (0.97-1.81)	>0.05
Once a day	1.34 (1.03-1.75)*	<0.05
>Once a day	1.45 (1.16-1.80)***	<0.001
Constant	0.07 (0.04-0.11)***	<0.001
Obesity		
Never	Ref RRR: 1	
1-2 days/week	3.89 (1.52-9.98)**	<0.01
3-6 days/week	1.66 (0.35-7.87)	>0.05
Once a day	2.39 (0.86-6.67)	>0.05
>Once a day	3.96 (1.50-10.47)***	<0.001
Constant	0.003 (0.00-0.02)***	<0.001

Conclusion

This study indicated that among UK children in the Millennium Cohort Study, there was a significant positive correlation between the frequency of artificially sweetened beverages and a rise in the risk of getting overweight and obese. The frequency of physical exercise and maternal education were discovered to be protective factors against the UK children's BMI growth.

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Authors Contribution

MBA: Conceptualization of Project
MBA: Data Collection
AR: Literature Search
MUS : Statistical Analysis
YL,SP: Drafting, Revision
MA: Writing of Manuscript

Correlation Between Computerized Tomography Severity Score and Patient Prognosis In Cases of Covid-19 Pneumonia: A Retrospective Study

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Abstract

Objective: To find the correlation between CT severity score and patient prognosis in cases of COVID-19 pneumonia in a tertiary care hospital in Lahore.

Method: It was a descriptive observational study, carried out at Chaudhary Muhammad Akram Teaching and Research Hospital, Lahore. We enrolled 80 patients clinically suspected of having COVID-19 pneumonia and showing characteristic HRCT features of the same, using consecutive sampling technique. Patient prognosis was classified into patients recovered and patients expired. A CT severity score (CTSS) consisting of 25 points was deployed to categorize disease as mild, moderate and severe. Statistical package for social sciences (SPSS) version 20 was utilized for statistical analysis. Association between patient prognosis and CT severity score of COVID -19 infection was studied by applying the Pearson correlation.

Results: Nineteen out of 19 (100%) patients with mild CTSS recovered, 32 (80%) out of 40 patients with moderate CTSS recovered while 8 (20%) expired and 11 (52.4%) out of 21 patients with severe CTSS recovered while 10 (47.6%) expired. A statistically significant positive correlation (p = 0.001) was observed between patient prognosis and CT severity score in COVID-19 patients.

Conclusion: A positive correlation exists between CT severity score and patient prognosis in cases of Covid-19 pneumonia.

Keywords: COVID-19, HRCT, CTSS , Pneumonia

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Introduction

Covid-19 spread quickly within weeks and months to become a pandemic, impacting the whole world population.[1] Globally, over 600 million covid-19 cases and over 6.5 million deaths have been confirmed till now.[2] Development of vaccines has slowed down the covid-19 infectivity rates; however, vaccine hesitancy and breakthrough infections still lead to many new cases. Emergence of new variants with higher transmissibility, also poses a continuous risk.[3,4] Covid-19 can present with variable severity and can involve multiple organ systems. Respiratory involvement is the most common feature in majority of the patients, and the disease severity can range from mild cough and flu-like symptoms to acute respiratory distress syndrome and multi-organ failure leading to death.[5,6] Reverse-transcriptase polymerase-chain-reaction (RT-PCR) of nasal swab is considered the diagnostic test of choice. This test has high specificity but only moderate sensitivity, and therefore not all the patients suffering from this disease are positive for this test.[7] High-resolution computed tomography (HRCT) of chest is an easy, noninvasive method with enhanced image resolution, and it has been conventionally used for evaluation of lung diseases. HRCT is not intended to be a diagnostic test but the sensitivity of radiologic findings on HRCT exceeds RT-PCR in even diagnosing Covid-19.[8] These

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findings include ground-glass opacity, consolidation, reticulations, interlobular septal thickening, crazy-paving pattern, linear opacities, sub-pleural curvilinear lines, bronchial wall thickening, lymph node enlargement, pleural and pericardial effusions. A combination of these findings can be presented as a semi-quantitative CT severity score (CTSS), which can help in assessing the radiologic severity of the pulmonary disease in these patients.[9] Different clinical features and laboratory parameters have been independently identified to be associated with worse outcome and death in covid-19 patients.[10] Considering that the pulmonary involvement is the common feature in most of the severe cases, evaluating the radiologic severity of the disease is very important in the context of patients' prognosis. Our study aims to evaluate the CTSS in covid-19 patients and their association with prognosis in our population. This can help the clinicians in correctly identifying the patients at higher risk of worse outcome and devising appropriate treatment strategies accordingly. The objective was to study correlation between CT severity score and patient prognosis in cases of Covid-19 pneumonia.

Material and Methods

This descriptive observational study was approved by ethical committee of Chaudhary Muhammad Akram Teaching and Research Hospital, Lahore. We enrolled 80 patients in our study utilizing consecutive sampling technique. Our study spanned over a period of 3 months from 1st January till 31st March, 2021. Patients aged between 20 to 90 years clinically suspected of having COVID-19 pneumonia and showing characteristic features of COVID-19 pneumonia on HRCT Chest were selected. Patient prognosis was categorized as recovered or expired. HRCT (chest) scans of patients were performed using 16 slice CT scanner. The 3 lung lobes on the right and 2 lobes on the left were individually assessed, and percentage involvement of the lobe was noted based on visual assessment. Visual severity scoring of CT chest was classified as score-1 (< 5% area involved), score-2 (5–25% area involved), score-3 (25–50% area involved), score-4 (50–75% area involved), score-5 (> 75% area involved), making the total score 25. A CTSS was assigned out of 25 based on the percentage area involved in each of the 5 lobes. The total CTSS is measured by the sum of the individual lobar scores and can range from 0 (no involvement) to 25 (maximum involvement), when all the five lobes show more than 75% involvement. CTSS consisting of a 25-point score was used to categorize radiological severity in each case as mild, moderate and severe. Involvement of each lobe was scored between 1 to 5 and scores from individual lobes were then added. A total score between 1 to 8 was considered mild, between 9 to 15 as moderate and more than 15 as severe. Clinical data of patients regarding duration of hospital stay, RT-PCR positivity or negativity and recovery/expiry was collected and documented on a preformed questionnaire. Data was then statistically analyzed using statistical package for social sciences (SPSS) version 20. Correlation between CTSS and prognosis of COVID -19 patients was studied by applying the Pearson correlation test.

Results

Out of the 80 patients 53.8% (n= 43) were male while 46.3% (n =37) were female. Mean age was 56.5 years ± 15 (range from 20 to 90 years). 62 (77.5 %) of patients were discharged from hospital whereas 18 (22.5%) expired during hospital stay. Majority of our patients remained admitted for 7 to 15 days. CTSS was mild in 19(23.8%) patients, moderate in 40 (50%) patients and severe in 21 (26.3%). The distribution of patients with respect to CTSS and other parameters is given in Table 1. A statistically significant positive correlation (0.001)

Table 3: *Comparison of Predictive Values (Bishop Score vs. Cervical Length)*

Parameters		CT severity score (CTSS)		
		Mild (Score 0-8) (N=19)	Moderate (Score 9-15) (N=40)	Severe (Score 16-25) (N=21)
Gender	Male (43)	12	22	09
	Female (37)	07	18	12
Age group	21-40 years (12)	04	06	02
	41-60 years (34)	08	17	09
	61-80 years (27)	07	10	10
	81-90 years (07)	00	07	00
Hospital stay	⩽ 15 days (67)	17	34	16
	> 15 days (13)	02	06	05
PCR result	Positive (69)	15	34	20
	Negative (11)	04	06	01
Prognosis	Recovered (62)	19	32	11
	Expired (18)	00	08	10

was observed between prognosis and CTSS score on applying the Pearson correlation, thus pointing towards a significant relationship between prognosis and CTSS in patients with COVID-19.

Discussion

In our study we analyzed the CT severity score of patients having characteristic features of COVID-19 pneumonia on HRCT chest in order to evaluate the role of CTSS in predicting the overall outcome of COVID-19 patients. CT scan has been used as a valuable tool in quantifying disease burden in patients of COVID-19 pneumonia.[11] CT severity can be quantified visually or by utilizing an automated software.[12,13] We used the visual scoring method in our study. Various scoring systems on CT comprising of 25 and 40 points have been utilized to categorize severity of COVID-19 pneumonia.[14] We used a 25 point scoring system in this study. Our study showed a positive correlation between CTSS and patient prognosis in terms of patient recovery and number of deaths. According to our study 100% of patients with mild CTSS recovered completely as compared to 80% with moderate score and 52.4% with severe score. On the other hand, none of the patients with mild CTSS expired while 20% and 47.6% patients with moderate and severe CTSS expired respectively indicating significant correlation between CTSS and patient outcome. These findings are in harmony with the previous relevant studies.[15,16] According to a study conducted in Abu Dhabi in 2020 there was significant correlation between CT severity score and length of hospital stay as well as clinical outcome. They concluded that patients with milder CT findings had positive outcomes, while increased death rate was observed among those having more severe CT changes.[17] These findings were reproduced in our study. Majority of our patients with moderate and severe CTSS were above 40 years of age indicating that more severe CT changes are associated with older age group. This is in agreement with study conducted by Al-Mosawe et al.[18] Many studies have reported a higher CTSS in male patients as compared to females while a few also reported lower mean CTSS in males[17,18,19,20], however we did not observe any significant correlation between higher/lower CTSS and male gender. This can possibly be attributed to smaller sample size and younger male patients in our study. Our study revealed that out of 80 patients having characteristic features of COVID-19 pneumonia on HRCT Chest 69 (86.25%) patients were RT-PCR positive while 11(13.75%) patients were RT-PCR negative. Similar results were documented by He et al. and Yang et al in their studies.[21,22] Furthermore, 78.9% patients with mild CTSS were RT-PCR positive as opposed to 85% and 95.2% in moderate and severe CTSS group respectively. This implies that patients with moderate to severe disease burden on CT are more likely to be RT-PCR positive as also stated by Al-Mosawe et al.[18] These findings also reflect the importance of HRCT chest as a screening and diagnostic tool for COVID-19 pneumonia especially in patients with mild disease. A similar study conducted by Fang et al. concluded that CT can be used for screening of COVID-19 in individuals clinically suspected of COVID-19 infection but showing negative RT-PCR test result.[23,24]

Conclusion

We conclude that there is a positive correlation between CT severity score and prognosis of COVID-19 patients in our population. CT Chest can also be utilized as a diagnostic tool where RT-PCR test results are inconclusive.

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Authors Contribution

TT: Conceptualization of Project
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MI: Writing of Manuscript

Approach and View of Medical Students toward Basic Medical Science Subjects: A Study at Bolan Medical College Quetta

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Abstract

Objective: To assess the view and approach of medical students towards basic medical science subjects beside its clinical relevance in Bolan Medical College Quetta Pakistan.

Method: This was a cross sectional study designed in Bolan Medical College Quetta Pakistan, from March-2021to May 2021. For collection of data pre tested questionnaire was used. All options were rated by using likert scale, ranges from strongly disagree to agree. The data were analyzed by using SPSS-27.

Result: A total of 200 students participated in this study. Among them 40 (20%), 55 (27.5%), 35 (17.5%), 35 (17.5%), and 35 (17.5%) were of 1st, 2nd, 3rd, 4th, and final year students respectively. 33 (16.5%) students were interested to join as career, 107(53.5%) were never join the basic side. Less financial attractions are in basic side by 130 (65%) that's why not interested. If modular system apply this may attract the students to join as career, the reply was in 65% (130) don't know. The clinical relevancy was 53.5% (107) anatomy, 47.5% (95) biochemistry while 41.5% (83) physiology.

Conclusion: This study concluded that students have very low attraction for basic medical science subjects but this can elevated with way of teaching methodology and using clinical aspect. Students are very much reluctant to join basic side as their career due to less financial attractions.

Key words: basic medical science, medical students, relevance, clinical

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Introduction

A number of science fields have been added to the existing medical science curriculum based on bio-medical subjects. The behavioral sciences and to some extend social sciences have been included in basic sciences, for making the base of medical students much stronger.[1] Initially the subjects of basic medical sciences are anatomy, physiology and biochemistry which mainly explains the sciences of functional, structural and bio-chemical properties of human body. These subjects are the major part of any medical curriculum and vital in understanding the clinical practices.[2] Various students of medical science refresh their clinical knowledge from their basic science medical knowledge. Though the role of basic medical science in learning the clinical practice has been contested often.[3] In Various institutes of medicine, advanced modified curriculum have been introduced, all of which have single or novel system curricula on problem based learning basis.[4] This part mainly focuses the student's approach towards problem based, integrated and clinically applicable methods of study.[5] This study technique boosts the active involvement of medical students and helps for lifelong learning and affection for basic medical science subjects.[6] The students who studied the usefulness of problem based learning found that the knowledge they have got from basic medical science study was very much constructive.[7]

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The basic medical science knowledge could be used to comprehend spontaneous tools of disease processes that advances and formulates the accuracy of diagnosis of diseases.[8] Meagre assimilation of basic medical sciences to clinical exercise through medical education may weaken the importance of these subjects.[9]

The knowledge of basic medical education can serve for enhanced understanding of clinical medicine and increases the basic learning.[10] Most undergraduate medical students casually expressed that their reminiscence of medical field in basic medical science is lesser than anticipated and that the content of those prescribed courses does not appear appropriate to their consequent clinical work or studies.[11] Some students think that basic sciences knowledge can only hinder in the progress of clinical work.[12] During rest of medical studies, the students slow[7] but increasingly develop negative views about basic sciences curriculum.[13] Some parts of South East Asia revealed the positive trend to develop more admiration for basic sciences in the medical students.[14] Research also proved that only few percentile of medical students keep the basic sciences subjects as their career specially the senior class students. Now a days students feel that extra curriculum made for basic sciences over tired their mental exertion which repel them to study the basic sciences.[15] In another US study revealed that avoiding to choose basic sciences as future career was their wish to become clinical specialist for better salary.[16] Many studies have been done on medical student's view on basic medical sciences globally but trend of under medical graduates in Pakistan is blurred on choosing basic sciences as career. During first couple of study years of medical students the retention rate of basic science subjects remained quite high but this becomes ambiguous during progress in clinical years.

Material and Methods

This cross sectional study was conducted in Bolan Medical College Quetta during the period of March, 2021-May, 2021. A predefined questionnaire was used for data collection. A short trial of questionnaire was conducted on small group of students' in February 2021, prior focusing research on full basis. Participants of this study were all students from first year to final year mbbs in Bolan Medical College Quetta during year 2021. Total of 200 students participated in this study. Questionnaire recollected after filling by students asking questions about basic science subject interests. Opinions rated according to positive point Likert scale. After completion the data were rechecked. Data were entered in SPSS version 26 for analysis. This analysis was descriptive to proceed for independent variables. Analysis of different opinions were done. Chi square test on variables performed and significance level of $P<0.05$ was fixed.

Results

A total of 200 students participated in this study. One hundred and fifty (75%) of all were in the age of 23-25 years. Most of the students 150 (75%) were male. Half of the students came from rural parts of the country. Almost all of the students were Muslims. Ninety (45%) students were interested in basic medical science subjects.

110 (55%) of students do not want to join the basic science subjects as career. Majority 140 (70%) of the students do not have to guide the juniors to join the basic side as career.

The reason for not joining basic side were amongst 120 (60%) due to less financial attraction with decreased promotion chances. Out of all students assessed, 160 (80%) of students agreed that basic medical science teachers do not encourage students to join this field. (Table-I)

Table 1: *Response of Students on Socio Demographic Perception*

Variables	Description	Frequency	Percentage
Age	18-22	25	12.5
	23-25	150	75
	26-30	25	12.5
Gender	Male	150	75
	Female	50	25
Resident	Urban	100	50
	Rural	100	50
Religion	Muslim	190	95
	Others	10	05
Student of year	First year	40	20
	Second year	55	27.5
	Third year	35	17.5
	Fourth year	35	17.5
	Final year	35	17.5

Amongst students asked for their interest in basic medical subjects, 45% of students showed for no interest. 35% have minimum and only 20% shown their interest in basic subjects.

Interest to join the basic side as career, majority 53.5% agreed on never join as career. While 30% replied may be and only 16.5% positively replied to join. On any

Table 2: *Medical Students' Interest and Perception to Basic Medical Science subjects*

Variables	Rate	Frequency	Percentage
Do you have any interest in Basic medical science subjects	Yes	40	20
	Minimum	70	35
	No	90	45
Interested to join as career	Yes	33	16.5
	Maybe	60	30
	Never	107	53.5
Do you advise juniors to join it as career	Sure	55	27.5
	Maybe	44	22
	Never	101	50.5
Why not to join Basic medical subject as career	Low financial growth	130	65
	No promotion	12	6
	Family pressure	19	9.5
	No clinicals	09	4.5
	Low society value	30	15
Basic science teacher encouragement is vital	Yes	70	35
	No	66	33
	Don't know	64	32
Financial attraction must be given to teachers	Yes	120	60
	No	80	40
Modular curriculum may increase the basic side attractions	Yes	23	11.5
	No	47	23.5
	Don't know	130	65

advice juniors to join it as career, 50.5% never advised their juniors for joining the basic side. 22% voted for maybe while 27.5% willing to give advice their juniors to join the basic medical subjects as career. On the question why not to join the basic side as career, majority 65% of the students replied in refusal due to low financial growth/ aspect. 6% replied for no promotion, 9.5% refusal due to any family pressure, 4.5% in no clinical practice and 15% in low or no favorable status in the society. The question of basic medical science teaching faculty's encouragement gives equal percentile by yes, no, don't know in 35, 33, and 32% for all. The financial attraction to the basic side faculty gives majority replies in 60% positively. The implementation of modular curriculum can confer good attraction, the reply was very strange in don't know (65%) by students. Overall the subject of anatomy given clinically relevant basic subject by 53.5% students. 8.5% students agreed on irrelevancy to clinical aspect of biochemistry. While the subject of physiology is moderately relevant to clinical side 56.5%. Chi-Square Test Comparison showed amongst total 200 respondents, majority (90%) of the students agreed on the subject anatomy as the lengthiest subject in both years of initial Profs. While the difficult one were physiology (78%). Students commented on anatomy as most interesting subject (88%) in both 1st

Table 3: *Clinical Significance of Basic Medical Subjects*

Subjects	Irrelevant		Moderately relevant		Highly relevant	
	Frequency	Percentage	Frequency	Percentage	Frequency	Percentage
Anatomy00		00	93	46.5	107	53.5
Biochemistry	17	8.5	88	44	95	47.5
Physiology	04	02	113	56.5	83	41.5

Table 4: *Chi-Square Test Comparison*

Variables	Anatomy			Physiology			Biochemistry		
	Frequency	percent	P value	Frequency	Percent	P value	Frequency	percent	P value
The course content is really extensive?	135	67.5	0.02	55	27.5	0.12	10	5	0.01
The subject entertains you during the study?	90	45	0.33	87	43.5	0.11	23	11.5	0.41
Knowledge of the subject is good for clinicians?	111	55.5	0.25	68	34	0.01	21	10.5	0.04
Basic subjects can cover clinical aspect without going into detail	77	38.5	0.04	66	33	0.13	57	28.5	0.01
Can these subjects confer you hints during clinical usage?	144	72	0.44	34	17	0.41	22	11	0.33
Can these subjects if integrated gives help in clinicals?	99	49.5	0.13	59	29.5	0.17	42	21	0.31
Do you think PBL can go a lot during clinical practices?	87	43.5	0.02	77	38.5	0.07	36	18	0.02

& 2nd years. Students considered the subject of physiology got the most (92%) connected with clinical subjects required for post-graduation. 90% of students argued in favor of anatomy in clinical surgery. The subject of biochemistry got low percentile (33%) to clinical touch by students. Most of the students (95%) entertained physiology as subject of help during the whole course work. (94%) students agreed on PBL- problem based learning can help in better understanding of the subjects' anatomy, physiology and biochemistry consequently (Table-IV).

Discussion

Problem based learning is an exclusive form of teaching committed to emerging students, self-learning with practicing skills. After several years of developing medical education, PBL has been recognized as the best in most of the medical institutes all over the world.[18]

This is quite clear that the subjects of basic medical science are prerequisite for other clinical science field which helps the clinical aspect of disease.[19] This study tried to discover the awareness and approach of medical students towards basic medical sciences with clinical significance. This study also tried in finding out the partialities about basic medical sciences as the future career and the motivation for students not being attracted in basic science subjects. This study revealed that only 20% of students were interested in basic sciences as career[20] This type of study conducted by kitajima et al which explored that a high percentage (74%) of medical students was keen interested to join basic sciences as career.[21] The same sort of study conducted in Japan where medical students manifested very low interest (24.7%) in basic sciences[22]. This is may be a difference in two medical institute's curriculum. Related to low interest of students to join basic sciences as future field, large number of students showed the reason of its financial aspect and very slow chances of promotion in such field. These findings were manifested in the studies conducted in China, Malaysia and South Asia. Very limited research, teachings, clinical aspect and laboratory works are the reasons why students are not taking any interest.[23] Many other studies have probed into these problems which explained as salaries and financial aspects are now envisaged as major factors that attracts the students to choose basic sciences as career, that's why students are more interested in clinical fields.[24] Moreover maximum number of students in this study still attracted to be good reputed clinician in future somewhat a researcher or basic medical science teacher. Many research conducted on medical students revealed that the knowledge obtained in clinical atmosphere to understand basic medical science given more understandings and attractions.[25] Majority of the students agreed on importance of combination of basic medical sciences with clinical subjects which helps in better understanding of subjects. This was very much clear in the study that that the subjects of anatomy and physiology were relevant regarding clinical field but biochemistry was irrelevant in its clinical aspect. The same study conducted with Australian medical students.[25] This difference of clinical relevance may be due to disparities in basic medical side teachers and methodology of teachings. If looks into the contents of the subjects, quite a number of students claimed about anatomy as the most exciting subject amongst all basic science subjects during studying 1st and 2nd year. This was endorsed in a study conducted in India.[26]

The resilience of basic medical science understandings has always been a substance of contention. A famous faith by physicians and medical researchers is that during clinical practices, the knowledge of basic medical science subjects which they got during their medical schooling is lost.[27] Students also apprehend the significance of PBL, with large number of students expressed that this could help in understanding their subject very well. However this methodology cannot conceal the whole syllabus, but other cohesive method may be used, with which few topics can be covered by traditional old way of teaching and rest by clinical way. A firm collaboration between basic and clinical departments with inspired faculty devoted to promote the excellence of medical education.[28-29]

Conclusion

This study concluded with the observations that students have very low attraction threshold for basic medical science subjects but this can be elevated by teaching methodology and clinical teachings. Students are very much reluctant to join basic side as their career due to less financial attractions. Anatomy and physiology remained good relevant subjects to clinical field. Better to incorporate the basic medical science subjects to clinical ones for understanding the knowledge.

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Authors Contribution

ZK: Conceptualization of Project
MM: Data Collection
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SJ: Statistical Analysis
ARZ: Drafting, Revision
AZ: Writing of Manuscript

Comparison of Early Re-Resection Versus Standard Surgical Method for Transurethral Resection of Urinary Bladder Tumor: A Randomized Controlled Trial

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Abstract

Objective: To compare results of early re-resection versus the standard surgical approach for bladder tumour transurethral resection.

Method: This 6-month randomized controlled at Urology ward Jinnah Hospital was conducted on 160 sample size calculated through WINPEPI software. Patients of bladder cancer were randomized into two groups , Group A had an early resection, within 6 weeks of the initial transurethral resection. Group B was without early re-resection. Patients were re-evaluated for tumour progression and recurrence at the resected site during follow-up. Data was entered and analyzed using SPSS version 20.0.

Results: In Group A 81% were males with 57.24+8.55 years mean age. In group B there were 90% males with mean age 54.39+8.26 years. In early re-resection group, 3 (3.8%) had tumor progression and 77 (96.3%) did not have tumor progression. In standard method group, 10 (12.5%) had tumor progression and 70 (87.5%) did not have tumor progression. Significant difference among two groups was observed. ($p<0.05$). In early re-resection group, 35 (43.8%) had recurrence of tumor and in standard method group, 55 (68.8%) had recurrence of tumor . The difference in both groups was significant ($p<0.05$).

Conclusion: Thus early re-resection (at 6 weeks) is beneficial in suppression of tumor progression and its recurrence as compared to standard method of resection which is done at three months.

Keywords: Re-resection, standard surgical method, transurethral resection, bladder tumor, tumor progression, recurrence

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Introduction

Urinary bladder cancer is 10th most common cancer worldwide and its incidence is rising especially in developed countries.[1] Most incidence occurs in between 40 -70 age group, with a men to women ratio of 3:1. More developed countries account for about 59 percent of bladder cancer cases. Southern, Western Europe and Northern America are with highest rates of bladder cancer, whereas middle Africa, central Asia, Latin America, and west Africa have the lowest rates.[2] Urinary increased frequency, urgency and lower urinary tract features are the commonly presented symptoms.[3] According to Karachi Cancer Registry (KCR), bladder cancer was the 4th most common cancer in males ant 5th in Females.[4] Bladder cancer known risk factors in addition to smoking cigarette are exposure to a number of industrial chemicals such as aniline dyes, painkiller (phenacetin) misuse, benzidine chemicals and catheters causing chronic irritation.[5]

The superficial tumors restricted to the bladder mucosa are classified as Ta or T1, with 20% of cases being classified as Ta, 70% as T1, and 10% as CIS.[4,5] The size of the tumor, multifocality, stage of the tumor, grade of the tumor, and early recurrence all influence disease progression.[6]

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With its varied behaviour, T1 grade 3 (T1G3) bladder carcinoma is one of the most difficult surgeries for urologists and patients alike.[7] Transurethral resection of bladder (TURBT) is considered as the gold standard treatment for these patients with bladder carcinoma (non-muscle invasive). Because the initial TURBT may not be enough to completely remove and stage the tumour, the risk of recurrence and advancement is raised. Non-muscle invasive bladder cancer (MNIBC) is widely known for having a high recurrence rate of >50 percent following initial resection. Reasons for this are incomplete resection and implantation of floating tumor cells.[8]

In usual practice, first TURBT is performed, and the patient is re- evaluated three months later for the second TURBT. However, according to European and American guidelines, the re-resection after initial TURBT should be performed within 2-6 weeks. The goal of early resection is to assure precise tumor staging, halt the cancer from progressing further, and thereby improve the prognosis.[9] According to one study, tumour recurrence rates were 35 percent and 42 percent, respectively, with and without re-resection. Patients who did not have early re-resection had significantly greater occurrence of progressive tumor stage during follow-up (late re-resection 14.4% vs. early re-resection 3.3%) (P<0.05).[10] The purpose of this research is to compare the results of early re-resection vs regular TURBT surgery. In comparison to normal protocol, literature has shown that re-resection within 6 weeks after initial resection had a superior outcome and prognosis for cancer patients. However, due to a lack of local evidence, it is not used in public sector settings. Furthermore, there is a scarcity of data in this area. We hope to obtain local proof that early re-resection of TURBT is a more useful and effective strategy for TURBT through this study. This will aid in the improvement of our practice, and in the future, we will use early resection as a therapy plan for patients with bladder cancer rather than a single TURBT.

Material and Methods

This is a randomized controlled trial conducted at Urology ward of Jinnah Hospital Lahore. A sample size of 160 cases was calculated, with 80 cases in each group, using a 5% threshold of significance, an 80 percent power of study, and the projected percentage of tumour advancement, which was 3.3 percent with early re-resection and 14.4% with the standard procedure. After approval from Ethical Review board of JHL/AIMC Candidates were chosen using a non-probability, purposive sampling method. Patients with bladder cancer who were 30-70 years old and of either gender were included. Bladder Carcinoma patients were randomly assigned two groups by using two folded cards (A & B) pickup method. Group A patients had an early resection, within 6 weeks of the initial transurethral resection. The conventional procedure was used in group B without re-resection. All of the procedures were carried out by a single surgical team with the help of the researcher. All of the procedures were carried out under spinal anaesthesia. Patients were then transferred to post-surgical wards and monitored there until discharge, as well as in the OPD. Patients were re-evaluated for tumour progression and recurrence at the resected site during follow-up. All of this data was entered into a proforma. SPSS version 20.0 was used to enter and analyse all of the data. The quantitative variables i.e. age (years), duration of diagnosis (months), tumor size (mm) were presented as mean ± standard deviation. The qualitative variables i.e. gender, recurrence or progression of tumor were analyzed and frequencies were calculated. Comparison among groups was done by using chi-square test. To assess statistical significance P-value≤ 0.05 was decided. Data was stratified for age, gender, duration of symptoms and tumor size. Chi square test was again performed post stratification.

Results

In group A 57.24+8.55 years was the mean age. In group B54.39+8.26 years was the mean age. In group A, there were 65 (81.3%) males and 15 (18.8%) were females. In group B, there were 72 (90%) males and 8 (10%) were females. In early re-resection group A, the mean duration of tumor was 20.35±9.90 days. In standard method group B, the mean duration of tumor was 31.70± 16.28 days. There were 80 (50%) who had tumor size <3cm and 80 (50%) had tumor size >3cm. (Table I) In early re-resection group A, there were 40 (50%) who had tumor size <3cm and 40 (50%) who had tumor size >3cm. In early re-resection group, 3(3.8%) had tumor progression and 77 (96.3%) did not have tumor progression. In standard method group B, 10(12.5%) had tumor progression and 70 (87.5%) did not have tumor progression. The difference in both groups was significant (p<0.05). In early re-resection group, 35 (43.8%) had recurrence of tumor and 45 (56.3%) did not have recurrence of tumor. In standard method group, 55 (68.8%) had recurrence of tumor and 25(31.3%) did not have recurrence of tumor. The difference in both groups was significant (p<0.05). (Table II) Data was stratified

for age of patients. On stratification, the difference regarding recurrence of tumor with respect to two operative procedures is significantly different in younger age group (35-50 years) as compared to old age group (51-70 years). Thus age has an effect on outcome of these procedures. Data was also stratified for duration and Size of Tumor. Results were statistically significant among those with less duration and smaller sized tumors. (Table-III)

Table 1: *Demographic and Disease Profile of Patients recruited in Standard (Group B) and Early Re-resection group (Group A). N= 180*

Variable		Group		Total
		Early Re-resection N= 80	Standard N=80	
Age	Mean	57.24 yrs	54.39 yrs	55.81 yrs
	Standard Deviation	8.55	8.26	8.50
Gender	Male	65 81.3%	72 90.0%	137 85.6%
	Female	15 18.8%	8 10.0%	23 14.4%
Duration of Symptoms	Mean	20.35 months	31.70 months	26.03 months
	Standard Deviation	9.90	16.28	14.59
Size of Tumor	< 3 cm	40 50.0%	40 50.0%	80 50.0%
	> 3 cm	40 50.0%	40 50.0%	80 50.0%

Table 2: *Comparison of Early Re-resection and Standard Method in terms of Tumor Progression and Recurrence*

Variable		Group		
		Early Re-resection N= 80	Standard method N= 80	
Tumor Progression	Yes	3 3.8%	10 12.5%	13 8.1%
	No	77 96.3%	70 87.5%	147 91.9%
	P Value = 0.043 (Statistically Significant)			
Recurrence of Tumor	Yes	35 43.8%	55 68.8%	90 56.3%
	No	45 56.3%	25 31.3%	70 43.8%
	P value = 0.001 (Statistically Significant)			

Discussion

TURBT is the first and most important step in the management of bladder tumors. This procedure has two pronged objectives. First is to determine histological diagnosis, and then to determine tumor stage and grade, and to achieve complete removal of non-muscle-invasive bladder tumors.[11] The point of concern is that results of transurethral resection are far from optimum, and the diagnosis and therapeutic purposes are not always achieved. The guidelines of European Association of Urology, recommend a second transurethral resection if there is suspicion that the initial resection was incomplete.[12] If patient has high grade bladder tumor with no involvement of muscle, second transurethral resection plays a vital role.[12] In our study, we observed that 3(3.8%)

Table 3: *Stratification Analysis to Control for Confounding by Age, Gender and Size of Tumor on Progression and Recurrence of Tumor among Early re-resection and Standard Method.*

Variable		Tumor Recurrence	Groups		P-Value	
			Early Re-resection (Group A)	Standard Method (Group B)		
Age (years)	35-50	Yes	4 20.0%	20 80.0%	0.000	Statistically significant in younger age group
	51-70	Yes	2 3.3%	4 7.3%	0.195	
Duration of Tumor (months)	10-30	Yes	34 44.2%	40 70.2%	0.003	Statistically significant in less duration group
	31-60	Yes	1 33%	15 65%	0.286	
Tumor Size	<3 cm	Yes	15 37.5%	31 77.5%	0.000	Statistically significant in smaller sized tumors
	>3 cm	Yes	20 50.0%	24 60.0%	0.369	

had tumor progression in early re-resection group while 10(12.5%) had tumor progression in standard method group. Also 35 (43.8%) who had recurrence of tumor in early re-resection group while in 55 (68.8%) who had recurrence of tumor in standard method group. The difference in both groups was significant ($p<0.05$) for both outcome variables. Vasdev et al conducted a trial and found that tumor recurrence was, respectively, 35% and 42% with and without re-resection. When follow-up was done, there was a statistically significant trend of tumor stage progression in patients who did not undergo early re-resection (Group B 14.4% vs. Group A 3.3%, $P < 0.05$).10 Our study has demonstrated slightly better results than Vasdev trial and both studies are demonstrating beneficial effect of early re-resection. This rate of residual disease is quite similar to the findings reported by Engelhardt et al to be 52% within an interval of eight weeks.[13] The major query to decide is regarding suitable interval to perform re-resection. Klan et al, has reported a rate of residual tumour of 43%. This study did not find any benefit to wait for two weeks or more from initial transurethral resection. Many studies on the other hand have advocated a delay of two to six weeks, to allow post-resection inflammatory change to settle facilitating better visualization and demarcation of tissues. Benefits of early re resection has also been documented by Lawrence Kim in 2020 and has also stated the effects of staging and size of tumor on outcome as mentioned in our study.[9] Our study results are in accordance with other published researches employing shorter re-resection intervals of four to six weeks and reporting residual tumour rates ranging from 33% to 62%.[9] In this study, the percentage of high grade tumors were only 10%. A recently published research advocates a re-resection at a gap of up to eight weeks and residual cancer was found in 66.7% of cases of pT1 tumors as mentioned by Han et al.[14] Upon stratification the outcome of both procedures was different with reference to tumor size. This finding is also supported by J C Chen as they showed a difference. But in our study cut off size was 3 cm and in Chen study it was 4 cm .[15]

Conclusion

Thus early re-resection (at 6 weeks) is beneficial in suppression of tumor progression and its recurrence as compared to standard method (resection done at three months). This will help in improving prognosis of patients and improve quality and longevity of life of patients.

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Authors Contribution

MA, SKB: Conceptualization of Project

SKB, AA: Data Collection

AA, MA: Literature Search

SKB: Statistical Analysis

NI, MY: Drafting, Revision

AA, SKB: Writing of Manuscript

Assessment of Learning Styles in Final Year Medical Students: Comparison of Private and Government Medical College

Naila Asad,[1] Nighat Nadeem[2]

Abstract

Objective: To make a comparison of preferred learning style of final year MBBS medical students of a private medical college with that of Government sector institution.

Method: Participants of this observational study were final year students of Services Institute of Medical Sciences Lahore (SIMS) and Lahore Medical and Dental College (LMDC) Pakistan. Fifty Final year students from each college filled the Visual Auditory Read/Write Kinaesthesia (VARK) Questionnaire. They were assessed according to their favorite method of learning and were classified as kinesthetic, visual, auditory, or read/write. Comparison of (VARK) scores between colleges was done by Independent Sample T-Test.

Results: There was no significant difference in preference of learning styles among students of both medical colleges. Majority students of both colleges preferred Unimodal style (LMDC-78% vs SIMS-74%). Multimodal style was seen in the rest of students. Read/writing was common among the students of both colleges (20%). Kinesthetic style was preferred by 34% of students of private vs 20% from Government institution.

Conclusion: Teaching should involve all sensory modality so that all types of students can actively participate in learning session.

Keywords: Learning styles, Medical students, Visual Auditory Read/Write Kinaesthesia (VARK)

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Introduction

Learning styles describes the association between student, context and task.[1] Medical students diversify in their approach to learning for processing information.[2] Learning style is the fusion of intellectual, affective, and physiological characters that gives information of perception, interaction and response of a learner to the learning environment.[3,4,5] It is the approach by which a student prefers to process, comprehend and retain knowledge.[6] Dunn et al defined it as different techniques used by students to learn and recall information.[7] As medical teachers we need a better understanding of students' approach to learning as it impacts the educational outcome.[8] Honey and Mumford classified learners as reflectors, activist, pragmatist and theorists. Neuro-linguistic Program theory recommended visual, auditory, read/write and kinesthetic style to learn.[9]

Learning styles have an influence on learning and performance. The learner does not realize his or her mode of learning. An effective and correct learning style can help student to gain achievement in better understanding.[10] Studies have shown that identifying learning styles can help in selection of teaching methods that can be most effective and will result in better performance and educational outcome.[5]

Variation among the learning style and teaching methodology is a basic reason for lack of interest by students. Thus, the teaching-learning process can be strengthened

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by detection of styles of learning and selecting the most suitable teaching methods.[11] Differences in learning process among students can promote deeper learning and improve the acquisition of knowledge, which is essential for the understanding and practice of medicine.[3] Research has shown significant value in aligning dominant learning styles of students and teaching styles of instructor for better academic performance.[12] The modalities of learning in students is assessed at a regular interval in most medical institutions. Thus the teachers become aware of their students' ability to learn.[10] Students' attention and motivation improve when the facilitator molds the lecture according to their ideal learning style.[13]

Studies done earlier have shown different modes of learning among medical students in different parts of the world. Various questionnaires have been used to assess the style to learning. In 1987, Neil Fleming developed The VARK questionnaire. It is a simple questionnaire that identifies four sensory modalities: visual, aural, read/write, and kinesthetic.[13] Students learn by diagram and charts in visual method and by listening to the information in aural modality. In read/write mode the primary way to assimilate knowledge is read and write. The kinesthetic learner uses practice and simulation for learning.[13] The creation of private medical colleges in Pakistan has given a chance to study in exclusive situations and presentation methods. Thus the teachers and students need to constantly update about the best ways of learning to bring a constructive change in medical education. This will help to identify students at risk and carry out attributional retraining along with teaching and learning methods to ensure achievement of deep learning and competency based outcome in these students. As the students entering in Private and Government medical colleges are from different schools, there is a need to know if there is a variation in their learning styles because of schooling system. Few studies are available in Pakistan comparing medical students of a government institution with a private institution. Thus, this study was conducted to determine and compare predominant preferred learning style of final year MBBS medical students of a private medical college with that of Government sector institution.

Materials and Method

This cross sectional study was conducted in Services Institute of Medical Sciences Lahore (SIMS) and Lahore Medical and Dental College (LMDC), Pakistan after approval of the Institutional Review Board. A sample size of 100 students was taken by non-probability purposive sampling technique. Fifty students of Final year from each medical college were included after written informed consent. VARK questionnaire 7.1 was used to assess the choice of learning style. It consisted of 16 multiple choice questions each having four options. Each option is associated with one of the following learning modes (visual, aural, read/write, kinesthetic). The students were asked to make one or more choices that best explained their preference. The preferred learning mode was indicated by the highest marks. The names were not recorded on questionnaire to preserve anonymity. VARK score were calculated and the preferences were obtained from the score. Those who had one preference were considered as unimodal learner. Bimodal learners were those who chose two preferences and those with three preferences were trimodal and lastly the quad-modal learners preferred all four components. SPSS V.25 was used to analyze the data statistically. Distribution of learning modes in students are expressed as percentages in each category. Scores of individual VARK components are expressed as mean ± SD. Comparison of VARK scores among the two institutions was done by independent sample T-test. $P<0.05$ was taken significant.

Results

Table 1 shows the mean score and standard deviation of each VARK component among the final year students of both medical colleges. Kinesthetic mode has the highest mean in students of the two medical colleges (5.48 vs 4.64) but it is not statistically significant.

No significant difference was seen in preference of learning styles among students of both private (Lahore Medical & Dental College) and Government sector medical colleges (Services Institute of Medical Sciences) ($p=>0.05$). Students of both medical colleges showed preference of unimodal learning style (LMDC-78% vs SIMS-74%). In multimodal category, Bimodal was the largest. 20% students of LMDC preferred bimodal style versus 16% students of SIMS. Trimodal style was seen in 6% students of SIMS while no student of LMDC preferred it. Quadmodal learning style was represented by 4% students of SIMS and 2% students of LMDC. (Figure. A & B) Among the unimodal group of private medical college (Lahore Medical and Dental College), majority preferred kinaesthetic (34%) followed by reading/ writing (20%), aural (18%) and the least preferred was visual (6%). Bimodal learners preferred six

combinations out of which read-kinesthetic was the most common (8%). Quadmodal learners were 2%. (Figure A & B) Students of Government medical college (Services Institute of Medical Sciences) who preferred unimodal style showed predominance of read/writing (22%). Equal percentage of students preferred aural and kinesthetic modality (20%) while 12% preferred visual learning. Read-kinesthetic mode was represented by 8% bimodal learners followed by quadmodal preference (4%). Preference of three combinations was seen in trimodal learners that was 2%.(Figure A & B)

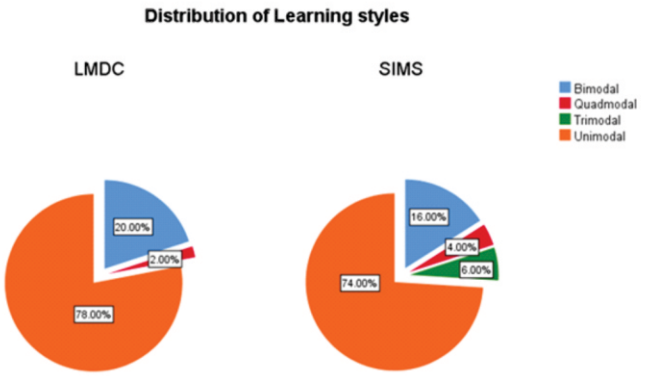

Figure A

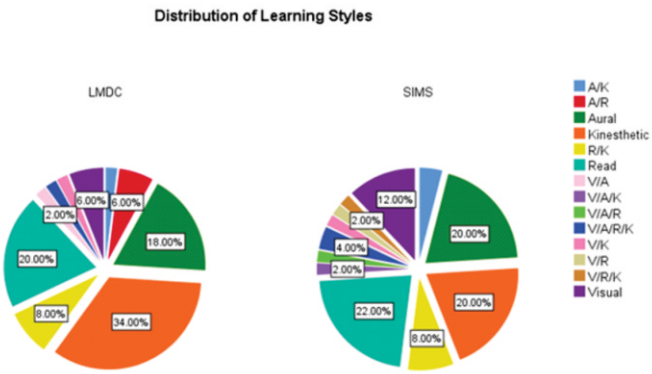

Figure B

Discussion

In Pakistan the present medical education system is changing from traditional teacher centered to active student centered learning. Active learning strategies promote thinking and improve the ability to identify problem and making a decision to solve it. Students learn in different ways to convert the information to long term memory. Knowledge and identification of learning styles may help teachers to solve learning problems in students and thus helping them to become effective learners.[10,14] This creates a better learning environment and help students to develop and use appropriate strategies in different medical situations.[12] The structure of education can be improved by recognition of different learning styles which will help teachers to modify their teaching methods according to the needs of students. This study was done to find the distribution of learning preferences in medical students of a private and Government sector college. The results of this study found that many students of both medical colleges selected to learn by one mode but the modalities were different. Kinesthetic mode was adapted by students of private medical college while preference was Read/Write style in Government sector medical college. The reason behind difference in preferred unimodal style in the two institutions may be due to teaching methodology used and learning environment. Another factor for this variation among the institutions could be the premedical education system as students are admitted from different schools. Bimodal learners were present in both medical colleges with read-kinesthetic mode being common among the students. This could be attributed to teaching of practical sessions as laboratory experiments, tutorials, anatomy dissections along with routine didactic lectures. Few quadmodal learners were observed in both colleges. Consistent with results of our study El Sayed et al also found unimodal learning style in Graduate

Table 1: *Group Statistics: Mean score of VARK Components.*

	Institution	N	Mean	Std. Deviation	Std. Error Mean
Visual	Lahore Medical & Dental College (LMDC)	50	3.70	1.787	.253
	Services Institute of Medical Sciences (SIMS)	50	3.80	1.863	.263
Aural	Lahore Medical & Dental College (LMDC)	50	4.34	2.488	.352
	Services Institute of Medical Sciences (SIMS)	50	4.52	2.384	.337
Read	Lahore Medical & Dental College (LMDC)	50	4.54	1.740	.246
	Services Institute of Medical Sciences (SIMS)	50	4.52	1.854	.262
Kinesthetic	Lahore Medical & Dental College (LMDC)	50	5.48	2.509	.355
	Services Institute of Medical Sciences (SIMS)	50	4.64	1.613	.228

year students of Inaya Medical College (70.9%). The difference was in mode of unimodal learners. 38% were aural learners as compared to kinesthetic and read/ write learners in our study.[10] Comparable to our results a study by Shahriki et al indicated Read/write to be the most preferred choice of learning.[11] In a similar study by Karthika on medical students of Government medical college, Central Kerala, single sensory modality was seen in 56.1%. Auditory style was preferred among students of unimodal style. 40.9% were multimodal and 3% bimodal.[14] Liew.SC et al reported unimodal (81.9%) was the preferred style and among unimodal 30% had kinaesthetic mode.[15]

In agreement to our findings, a study conducted by Razeqalla et al at the College of Medicine, University of Bisha, Saudi Arabia categorized learning patterns into unimodal (86.2%) and multimodal (13.2%). The difference was in dominant learning style. 55.9% students used aural as their preferred learning mode and 32.2% were kinesthetic while visual was the least presented (6.8%). As data was collected from male students only so that could be reason for the variation in dominant learning style in our study.[16] Fahim A et al studied the distribution of learning style in medical students and found unimodal style to be predominant in 39.37% (580) and 60.62% (893) to be multimodal.[17] Qahtani et al distributed a survey among the dental undergraduate students of King Saud Medical University and found unimodal learning preference in 38% of final year students.[18]

Different results have been published earlier regarding dominant style of learning. Chaudhry MH et al assessed the preferred learning styles and determined their association with the academic performance of 597 undergraduate medical students in various medical colleges in Pakistan. In contrast to our study results, they found unimodal modality in 27.6% students. Most preferred single mode of learning was auditory (10%) followed by kinesthetic (8.4%), visual (6%) and read/write (3%).[5] The reason could be the participation of all medical students in a college while our study was confined to only the Final year participants.

A study by Chouhan N et al on medical students of a college in Jammu revealed 53% to be multimodal and 47% adopted a single sensory modality to learn. They found 31%, 21% and 1 % were bimodal, trimodal and quadmodal, respectively.[19] Marzo et al studied clinical students of three medical colleges in Malaysia and found unimodal learning in 45.07% and remaining 54.93% preferred multimodal learning. Regarding multimodal learning style bimodal was preferred in 52.6%.[20] This variation from our study could be due to vast involvement of students in new technology. In a study by Nagesh et al, 73% of final year students preferred multimodal learning versus 27% who were unimodal. He also found that kinesthetic style was most common among students.[21] Sinha et al in his study on medical students of Malaysian medical college showed that 45% were monomodal and 55% were multimodal. In monomodal category kinesthetic preference was strongest (45%) in students.[22] Daud S et al analysed students of first year to fourth year and found unimodal style in 31% and multimodal in 69%. The dominant style was aural (14%) in unimodal learners which was followed by kinesthetic (13%).[23] A study by Bokhari et al revealed majority (13.4%) of final year students of Sialkot medical college, Pakistan were multimodal and 5% were unimodal. 31.26% of these multimodal learners were in favor of kinesthetic learning.[24] The differences observed from our study may be due to the preparatory classes before entering the medical school.

The findings of the current study provided an insight into ways that our medical students learn in different medical colleges. Majority favored kinesthetic and read/ write followed by aural in unimodal learners. Read-kinesthetic was common among the six combinations of bimodal learners. This showed that how students have different approaches to make their brains work during learning. In this study we did not provide students with specific teaching and learning methodologies that were according to their learning preference styles. Teachers and facilitators need to familiarize with all modes of learning modes to capture the interest of students and to maximize learning and outcome. They need to adapt active strategies that could benefit all types of learners and will facilitate better learning process.

Certain limitations of our study were that we did not compare the preference of learning style among males and females. Also the influence of learning style on academic performance was not determined. Future studies can be done regarding this taking a larger sample size.

Conclusion

According to results of this study, students of the two different institutions did not show significant difference in the modes of learning. Unimodal learning style is preferred by majority of medical students though the

choice of modality is different among them. There is a need to conform instructional methods according to the learning styles. This will make learning better and might enhance student's performance.

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Funding Source *None*

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Authors Contribution

NA: Conceptualization of Project
NN: Data Collection
NA: Literature Search
NA: Statistical Analysis
NA: Drafting, Revision
NA: Writing of Manuscript

The Risk Factors of Diabetic Neuropathy in Type 2 Diabetic Patients Presenting to Services Hospital Lahore

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Abstract

Objective: To investigate the risk factors and to study the effect of these risk factors on the diabetic neuropathy (DN).

Method: The study was a retrospective case-control, hospital-based study and was carried out from18th November 2021 to 20th December 2021 through the questionnaire. Respondents were patients of diabetes mellitus (n=277) who visited the Diabetes Management Center of Services Hospital, Lahore. Binary Logistic regression model was fitted using SPSS 20.0

Result: Sample comprised of 277 subjects and among these, 122 and 155 were cases and controls respectively. Female gender (OR=2.225), duration of diabetes (OR=1.066), blood glucose level in fasting (OR=1.006), and age (OR= 1.042) have a significant effect on the prevalence of diabetic neuropathy.

Conclusion: The risk of Diabetic Neuropathy has been found higher, due to an increase in age, duration of diabetes and uncontrolled glucose level in the blood. Female patients of diabetes mellitus have higher probability of DN as compared to male patients.

Keywords: Type 2 diabetes; Diabetic Neuropathy (DN); Diabetes Mellitus (DM)

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Introduction

Among non-transmissible diseases, diabetes mellitus (DM) has growing economic burden in both developing and developed countries on individuals and on public health care system. In Pakistan, the annual direct and indirect cost estimated to manage diabetes in 2022 was 740.1 USD.[1] Almost 4 out of 5 (79%) adults who had diabetes belonged to "low or middle income countries". Globally, almost 33% of elderly population (65 or older) is diabetic.[2] It is a fact that 50% of diabetic patients remained undiagnosed.[3] In Southeast Asian countries, 80 million population suffered from diabetes and it is forecasted that it can rise to 151 million by 2045.[4] In Pakistan, 11% population had diabetes in 2011 and it is estimated to increase up to 15% till 2030.[4] Another study reported that prevalence of diabetes will be expected to be doubled (7 million to 14 million) by 2040 in Pakistan.[5] Pakistan, stands at 7th number globally regarding prevalence of diabetes mellitus and if it rise at same level it can reach to 4th in ranking.[4] About 48,800 Pakistanis aged 30-69 and 47700 aged >70 died due to diabetes or due to related complications.[5] Health care experts and those who formulate policies have to identify strategies to encounter this situation and take effective interventions to lower down its prevalence rate.[6]

Diabetic neuropathy is one of the common complication of diabetes mellitus. Diabetic Peripheral Neuropathy (DPN) is defined as "It is a symmetrical, length-dependent sensorimotor polyneuropathy attributable to metabolic and micro vessel alterations as a result of chronic hyperglycemia exposure".[7] Globally, 60% to 70% of the diabetic patients suffered from Diabetic Peripheral

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Neuropathy DPN.[8] Diabetic neuropathy creates many complications in different organs of body. It causes harm to nerves, generates sleep and mood disorders and has negative impact on the routine of life. It damages and compromises overall quality of life of the person suffering from this problem. Chances of foot ulcer and charcot joints are more in case of peripheral neuropathy. Peripheral neuropathy may result in morbidity and mortality. Autonomic neuropathy may result in gastric, diarrhea, constipation, bladder, myocardial infraction, arrhythmia, erectile dysfunction and fertility complications.[9] Sometimes it becomes reason of sudden death. Diabetic patients who experience loss of sense, numbness and aches are categorized as suffering from sensorimotor neuropathy.[10]

Age, hyperglycemia, hypertension, duration of DM, smoking, obesity, hyperinsulinemia and dyslipidemia are risk factors of diabetic neuropathy.[11] Progression of diabetic neuropathy can be reduced if controllable risks factors are identified that significantly affect the diabetic patients with particular social and economic background of our region. Early stage screening of diabetic neuropathy curtails the adverse impact of complications. This early screening may be helpful in lowering risk of foot ulcer.[8] In developing countries, health care facilities to look after diabetic neuropathy are either not accessible or affordable. In low resource settings, early identification of diabetic neuropathy and its associated risk factor can be helpful in minimizing the burden of disease.

Materials and Methods

The survey-based retrospective study has been conducted in the Diabetes Management Center of Services Hospital, Lahore. The data had been collected from 277 patients who visited the center from 18th November 2021 to 20th December 2021 through the questionnaire. 122 Patients with the manifestation of any type of diabetic neuropathy are taken as cases and the other 155 who did not suffer from neuropathy are considered as control. The main aim of this study is to determine the risk factors of diabetic neuropathy in type 2 diabetes patients. The response variable (diabetic neuropathy) is binary (yes or no). Potential risk factors age, gender, blood sugar level, and blood pressure level are continuous variables and BMI, smoking status, family history, thyroid history, occupation, treatment approach, and physical activity have been taken in the study through extensive literature review on the same research. In this study, SPSS version 20.0 was used for the analysis purpose. BMI is categorized as normal (18.5 to 22.9), over weight (23 to 24.9) and obese (25 or more).[12] Blood sugar level in fasting is taken as low (less than 80), normal (80 to 130) and high (more than 130). Blood sugar level in any time of day(random) is classified as low (less 90), normal (90 to 180) and high (more then 180). Blood pressure (upper/lower) is identified as low (90/60), normal (120/ 80) and high (130/more than 80). The chi-square test is used to test the association between outcome variables i.e. diabetic neuropathy (Yes, No) with different socioeconomic, demographic and clinical factors. The chi-square statistic [11] is computed as:

$$\chi^2 = \Sigma_i \Sigma_j \frac{(n_{ij} - u_{ij})^2}{u_{ij}}$$

Logistic regression is used to study the effect of risk factors on binary dependent variable. In current study diabetic neuropathy is dichotomous (yes, no) that leads to the choice of binary logistic regression model. Model is used to predict the chances of occurrence of an event of interest. The mathematical form of model is given as following:

$$\boldsymbol{Y}_i = \beta\boldsymbol{0} + \beta_i \boldsymbol{X}_i + \varepsilon_i$$

$$P(Y/X) = \frac{e^{\beta_0 + \beta_1 X}}{1+e^{\beta_0 + \beta_1 X}}$$

$$\ln\left(\frac{P(Y \mid X)}{1 - P(Y \mid X)}\right) = \beta_0 + \beta_1 X$$

$$E(Y) = \frac{e^{\beta_0 + \beta_i X_i}}{1+e^{\beta_0 + \beta_i X_i}}$$

Consider the p risk factors denoted by the vector $x_i = (x_1, x_2, x_3 ..., x_p)$. The conditional probability that the outcome of interest is present is given as:

$$\ln\left(\frac{p}{1-p}\right) = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + ... + \beta_p X_p$$

$$g(x) = \beta_0 + \beta_1 X_1 + ... + \beta_p X_p$$

Results

In this study, bar charts and percentages are used for data exploration. Results and interpretation of descriptive and analytic section are documented in this section. Among 277 diabetic patients, 44% (122/277*100) suffered from diabetic neuropathy. Retinopathy, nephropathy, stroke, ischemic heart disease, hyperlipidaemia, chronic liver disease, malignancy were found rare in

study participant, where hypertension and intermittent claudication are common complications related to type 2 diabetic patients in this study. None of the patient have been found suffering from pulmonary tuberculosis (TB) and uremia.

Numbness and burning are found very common symptoms of diabetic neuropathy in type 2 patients, where cold, tingling, dull pain, cold pain are rare in patients. Sensitivity is also present in those who have severity of diabetic neuropathy.

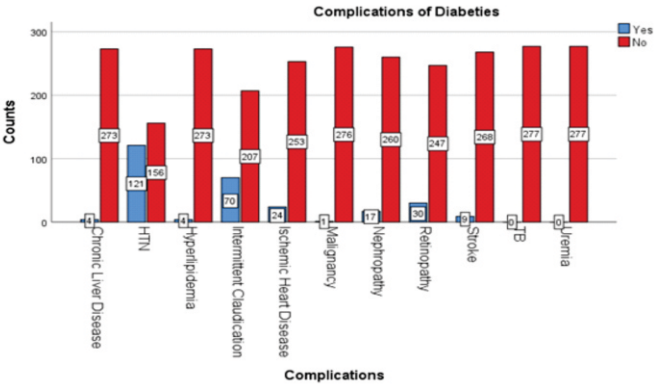

Fig-1: *Prevalence of complications in type 2 Diabetes Patient Other than Diabetic Neuropathy.*

Table 1: *Percentage (Frequency) Distribution of Demographic and Clinical Factors of Study Participants*

Variable	Categories	Percentages(n)
Gender	Male	52.5% (145)
	Female	47.7% (132)
Age	<50	47.7% (132)
	50-69	49.5% (137)
	⩾70	2.9% (8)
Sugar Level (Random)	Low	1.1% (3)
	Normal	19.1% (53)
	High	79.8% (221)
Sugar Level (Fasting)	Low	0.7% (2)
	Normal	23.5% (65)
	High	75.8% (210)
Duration of Diabetes (years)	<5	50.2% (139)
	5-11	30.7% (85)
	⩾12	19.1%(53)
BMI	Normal	11.6% (32)
	Over Weight	11.6% (32)
	Obese	76.9% (213)
Blood Pressure (Upper)	Low	1.8% (5)
	Normal	23,1% (64)
	High	75.1%(208)
Blood Pressure (Lower)	Low	1.8% (5)
	Normal	50.2% (139)
	High	48%(133)
Smoking Status	Yes	8.3% (23)
	No	91.7%(254)
No. of Times Sugar Level Checked in Last Month	⩽ 10	57.8% (160)
	11-29	29.2% (81)
	⩾30	13% (36)

Variable	Categories	Percentages(n)
Occupation	Do not Work	56%(155)
	Non Professional	20.9%(58)
	Professional	23.1%(64)
Treatment for Diabetes	Insulin	43.3% (120)
	Oral Hypoglycaemia (OH)	35% (97)
	Both Insulin and OH	13.7% (38)
	No Medicine	7.9% (22)
Working Status	Not Employed	55.2% (153)
	Employed	37.9% (105)
	Retired	6.9% (19)
Visiting Diabetic Centre	Yes	94.9% (263)
	No	5.1% (14)
No. of Visits in Diabetic Centre in a Year	No Visit	5.4% (15)
	1- 3	65.7% (182)
	⩾4	28.9% (80)
Admitted in Hospital Due to Diabetes	Never	84.1% (233)
	1-2	12.6% (35)
	⩾3	3.2% (9)
Drug History	Yes	0.4% (1)
	No	99.6% (276)
Knowledge About Diabetes	Yes	59.6% (165)
	No	40.4%(112)
Family History of Diabetes	Yes	57% (158)
	No	43% (119)
Thyroid (Hyper/Hypo) History	Yes	4% (11)
	No	96% (266)
Physical Activity	Regular	48.0% (133)
	Not Regular	42.6%(188)
	Not any Activity	9.4%(26)

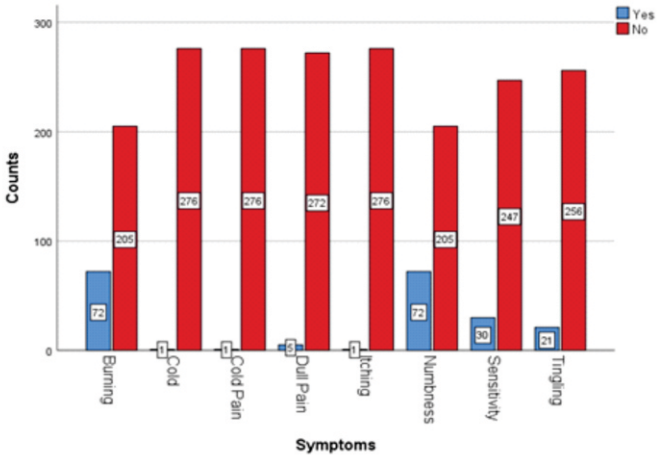

Figure 2: *Symptoms of Diabetic Neuropathy in Type 2 Diabetic Patients*

Gender, age, duration of diabetes, smoking status, occupation, working status, number of visits to doctor/ diabetic clinic in a year, admitted in hospital due to diabetes and physical activity were found significantly associated with diabetic neuropathy **(Table 2)**.

Odd ratios computed from binary logistic regression model have been reported in Table 3 using backward elimination method for selection of significant predictors. Gender, duration of diabetes, age and blood sugar level (in fasting) has shown significant relationship with diabetic neuropathy in type 2 diabetic patients. The probability of diabetic neuropathy is increased by 4.2% (OR=1.042; CI= 1.238, 3.998) for per year increase in the age of type 2 diabetic patient. Per year increase in the duration of diabetes increased the risk of occurrence of diabetic neuropathy by 6.6% (OR= 1.066; CI=1.0616, 1.116). The chances of diabetic

Table 2: *Percentage Distribution of Risk Factors × Diabetic Neuropathy*

Risk Factors	Categories	Neuropathy		χ^2
		Yes	No	
Gender	Male	31.1%	68.9%	17.246*
	Female	55.9%	44.1%	(0.000)
Age	< 50	36.4%	63.6%	6.664*
	50-69	51.8%	48.2%	(0.036)
	>70	44.0%	56.0%	
BMI	Normal	37.5%	62.5%	2.282
	Over weight	34.4%	65.6%	(0.319)
	Obese	46.5%	53.5%	
Duration of Diabetes (years)	<5	30.9%	69.1%	18.493*
	5-11	58.8%	41.2%	(0.000)
	⩾12	54.7%	45.3%	
Sugar Level (Fasting)	Low	0%	100%	-
	Normal	33.8%	66.2%	
	High	47.6%	52.4%	
Knowledge about Diabetes	Yes	40.2%	59.8%	1.140
	No	46.7%	53.3%	(0.286)
Smoking Status	Yes	17.4%	82.6%	7.229*
	No	46.5%	53.5%	(0.007)
Sugar Level (Random)	Low	0%	100%	-
	Normal	30.2%	69.8%	
	High	48.5%	52/0%	
Blood Pressure (Upper)	Low	___	___	0.203
	Normal	46.4%	53.6%	(0.652)
	High	43.3%	56.7%	
Blood Pressure (Lower)	Low	80.0%	20.0%	2.677
	Normal	43.2%	56.8%	(0.262)
	High	43.6%	56.4%	
Visiting a Diabetic Centre	Yes	44.1%	55.9%	0.008
	No	42.9%	57.1%	(0.927)

Risk Factors	Categories	Neuropathy		χ^2
		Yes	No	
Drug History	Yes	100%	0%	-
	No	43.8%	56.2%	
Occupation	Do not work	56.1%	43.9%	21.104*
	Non Professional	26.6%	73.4%	(0.000)
	Professional	31.0%	69.0%	
Working Status	Not Employed	53.6%	46.4%	18.636*
	Employed	27.6%	72.4%	(0.000)
	Retired	57.9%	42.1%	
Treatment for Diabetes	Insulin	46.7%	53.3%	3.517
	Oral Hypoglycaemia OH)	42.3%	57.7%	(0.319)
	Both (Insulin and OH)	50.0%	50.0%	
	No Medicine	27.3%	72.7%	
Family History of Diabetes	Yes	41.1%	58.9%	1.259
	No	47.9%	52.1%	(0.262)
History of Thyroid (Hyper/Hypo)	Yes	36.4%	63.6%	0.274
	No	44.4%	55.6%	(0.601)
No. of Times Sugar Level Checked in Last Month	⩽10	40.6%	59.4%	1.843
	11-29	49.4%	50.6%	(0.398)
	⩾30	47.2%	52.85	
No. of Visits in Diabetic Centre in a Year	No Visit	40.0%	60.0%	7.163*
	1-3	40.5%	59.5%	(0.028)
	⩾4	61.7%	38.3%	
Admitted in Hospital due to Diabetes	Never	40.8%	59.2%	7.604*
	1-2	57.1%	42.9%	(0.022)
	⩾3	77.8%	22.2%	
Physical Activity	Regular	43.6%	56.4%	7.929*
	Not Regular	39.6%	61.0%	(0.019)
	No Activity	69.2%	30.8	

– is used in Table 2 as chi square is not computed if any cell frequency is "0", * significant at 5%

neuropathy is increased by 0.6% for per unit increase in blood glucose level in fasting. Females have almost a twice risk of having diabetic neuropathy as compared to the male type 2 diabetic patient (OR=2.225 CI= 1.238, 3.998).

Table 3: *Odd Ratios of Significant Factors of Diabetic Neuropathy using Binary Logistic Regression Model*

Risk Factors	OR	P-value	95%CI	
			Lower	Upper
Gender (ref. male)	—	—	—	—
Female	2.225	0.008	1.238	3.998
Duration of diabetes	1.066	0.009	1.0616	1.116
Age	1.042	0.001	1.016	1.068
Blood sugar level (fasting)	1.006	0.002	1.002	1.010

Discussion

Knowledge about risk factors of diabetic neuropathy (DP) helps to control its prevalence. Diabetic neuropathy (DN) has different types like diabetic peripheral neuropathy (DPN), proximal neuropathy, autonomic neuropathy, and sensorimotor neuropathy. This study was conducted to determine the risk factors of diabetic neuropathy and investigated its effect on developing DN. Age, gender, duration of diabetes, and unbalanced glucose level in fasting has shown significant association in developing diabetic neuropathy in type 2 diabetic patients. It is widely accepted that older age, long-duration diabetes, and poor glycemic control are important risk factors in DN development.[13] In this study, the age group 50 to 69 has a large number of people suffering from DN. Another study conducted in Lahore had shown that this particular age group has a large number of diabetic peripheral neuropathy patients and age had also shown a significant association with DPN.[14] The cross-sectional study, previously conducted at the Diabetic Management Center (DMC) of Services Hospital Lahore indicated that age had a significant effect on sensorimotor neuropathy.[15] In the research conducted in India, it has been also shown that the age wise prevalence of diabetic neuropathy for age groups 50 to 59 and 60 to 69 was found at 43.6% and 52.9% respectively.[16]

It is also observed in current study that as the duration of diabetes increases the prevalence of diabetic neuropathy also increases. Similar results were found in some other studies in which peripheral neuropathy and sensorimotor neuropathy showed positive significance in duration of diabetes.[14,15] In a recent study unbalanced glucose level in fasting has a positive significant effect on prevalence of diabetic neuropathy. These results are in line with previous research in which uncontrolled glucose level in fasting is significantly associated with sensorimotor neuropathy.[15] A study conducted in 14 countries on diabetic peripheral neuropathy had shown that the risk of DPN is increased due to poor glycemic control.[17] The current study revealed that the female type 2 diabetes patient (n=132) has 55.9% diabetic neuropathy cases present while male type 2 diabetic patient (n=145) has 31.1% diabetic neuropathy cases found. The probability of DN is twice as higher in female type 2 diabetic patients as compared to the male type 2 diabetic patients The Cross-Sectional study conducted in Services Institute of Medical Sciences, Lahore, indicated that 21.25% of males with type 2 diabetic patients (n=80) suffered from DPN and 20% of type 2 diabetic females (n=70) faced problem of DPN.[18] In research, males have a large number of cases of DPN but carpal tunnel syndrome (CTS) in females is more frequent.[19] CTS may become the cause of numbness and pain in the finger. These symptoms of DN are found very common in current study so that might be the cause of the significantly higher risk of DN in females.

Conclusion

Risk of diabetic neuropathy significantly increased due to increase in age, duration of diabetes, uncontrolled glucose level in the blood. The chances of diabetic neuropathy is found twice for female diabetic patients as compared to male diabetic patients. Studies should be conducted to reduce burden of diabetic neuropathy by creating awareness among female and aged patients to control their glucose level.

Conflict of interest *None*

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Authors Contribution

AK, MI: Conceptualization of Project
SA, MI, KM: Data Collection
SA, AK: Literature Search
AK, SA, AS: Statistical Analysis
AK, SA, AK, MI, KM: Drafting, Revision
AK, SA, AK, AS : Writing of Manuscript

Correlation Between Hand Length And Stature

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Abstract

Objective: The main objective is to know the correlation between hand length and height so that a regression equation could be obtained to use for personal identification.

Method: It was a correlational study. Study center was at Sialkot medical college. Study duration was three months i.e., from April 2022 to June 2022. Only female students of Sialkot medical college were selected by non-probability purposive sampling technique. Sample size was 141. Those having any deformity of vertebral column and hand deformity were not selected. After taking informed consent measurements were taken. Stadiometer was used to measure the height and vernier caliber was used to measure hand length. The measurements were taken in inches. Descriptive data was calculated by using SPSS 25. Pearson correlation coefficient was found and regression equation was obtained. Regression curve was also obtained. Graphs and table were formed.

Results: Value of r between RHL and height was 0.780 and between LHL and height was 0.752. Conclusion: Hand length can be used to estimate height of the person helping to short list the persons to be identified.

Keywords: Linear regression, pearson correlation coefficient, regression curve, Height

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Introduction

For the purpose of art of making pictures calculating measurements of various parts of the body has been used since hundreds of years before Christ. Later on in seventeenth century it was used in medical profession.[1] Different biological characteristics used to help get positive identification, like standing height and weight also help to get information about growing up of children related to their upbringing depending upon their balanced diet. It helps in assessing body surface area.[2] Short height has more chances of developing faster heart rate. A single regression equation cannot be used universally because sex and environment impacts the length and breadth of hand. These measurements can be used to predict the height of a person.[3]

Height also helps to assess normal physical growth of the children and young and effects of balanced diet on different biological characteristics of a person.[4,5] It is easy to measure standing height if a person is free from any deformity of vertebral column, disease or lose of limb. But in these conditions standing height cannot be obtained then other reliable way can be used to estimate standing height like by measuring hand length, foot dimensions, length of various bones and different dimensions of other parts of the body.[6] Various measurements of hand give a dependable source to estimate standing height and give a predicted value very close to actual height.[7,8] To construct standing height different body parts, play a pivotal part like spinal bones, lower limb, and head. They are different for people living in different geographical areas of the world[9]. There are two main methods utilized to estimate height i.e., anatomical and mathematical. The second method derives estimation of height either by regression equation or multiplication factor. In forensic medicine when only a part of body is available as a result of disaster.[10] regression equation

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can be reliably used to estimate height. In a study carried out in India a very strong and statistically positive correlation was found between hand length and height.[11] In another study value of r was found to be 0.639 in males and 0.571 in females.[12] In India a study carried out in Karnatka concluded that there is very weak relationship between height and hand length with 0.25 value of r.[13]

Material and Methods

It was a correlational study. Study center was at Sialkot medical college. Study duration was three months i.e., from April 2022 to June. Only female students of Sialkot medical college were selected by non-probability purposive sampling technique. Sample size was calculated by using correlation formula. Sample size was 141. Those having any deformity of vertebral column and hand were not selected. After taking informed consent measurements were taken.

One female student was trained to take the measurements. All measurements were taken in college hours. Every student was asked to put off her shoes and stand against the wall by keeping her feet adjacent to each other. Stadiometer was used to measure the standing height from top of head to the floor. Hand length was taken from tip of middle finger when hand was placed in adduction on the plane surface of the table, to the crease of the hand. Vernier calipper was used to measure hand length.

The measurements were taken in inches. Descriptive data was calculated by using SPSS 25. Pearson correlation coefficient was calculated and regression equation was obtained. Reg-ression curve was also obtained. P value was 0.05. Graphs and table were formed.

Results

One hundred and forty-one female students were selected to take measurements. The least height was 59.40 inches, maximum height was 66.50 and mean height was 63.26 inches. As depicted in **(Table-1**). Value of pearson correlation coefficient between height and right hand length and left hand length is depicted in **(Table-2**). It is 0.780 and 0.752 respectively for RHL and LHL. Regression curve along with regression equation between height and right hand length has been depicted in the (Fig-1). Regression curve along with regression equation between height and left hand length has been depicted in the **(Fig-2)**.

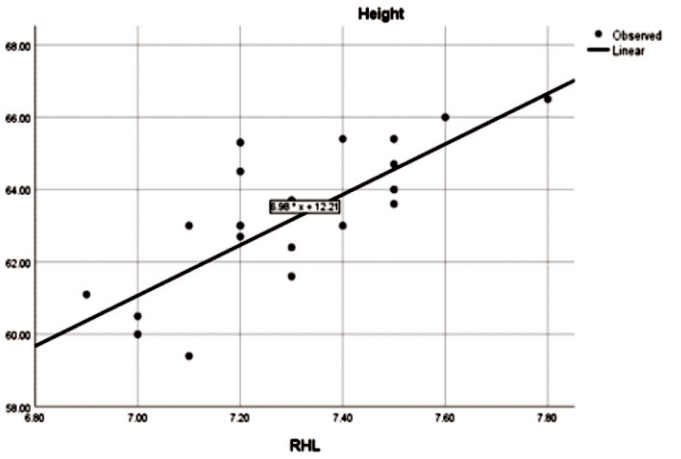

Fig-1: *Regression Curve and Equation Between Height and RHL.*

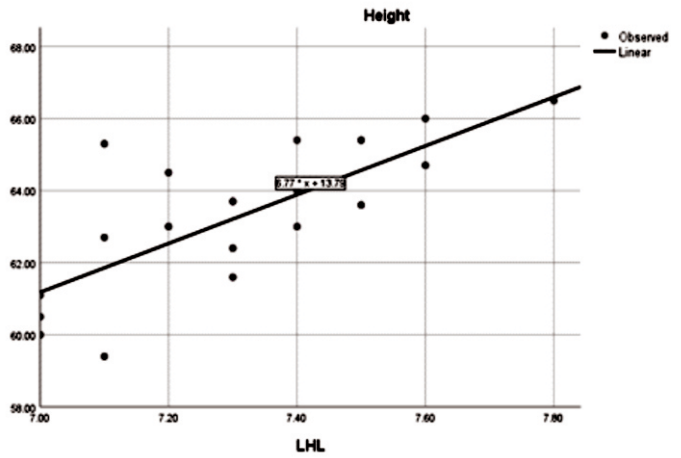

Fig-2: *Regression Curve and Equation between Height and LHL.*

Table 1: *Data describing minimum, maximum and mean values of all variables.*

	N	Minimum	Maximum	Mean	Std. Deviation
Height	141	59.40	66.50	63.2610	±1.86420
RHL	141	6.90	7.80	7.3085	±.20822
LHL	141	7.00	7.80	7.3064	±.20709

Table 2: *Value of r & F along with p value*

	Value of r	P value
Height and Right hand length	0.780	0.000
Height and Left hand length	0.752	**0.000**
	Value of F	**P value**
Height and Right hand length	216.2	0.000
Height and Left hand length	181.12	0.000

Table 3: *Value of t of regression coefficients has been depicted in*

	Value of t	P value
Height and Right hand length		
constant	3.516	.001
Right hand length	14.704	.000
Height and Left hand length		
constant	3.750	.000
Left hand length	13.458	.000

Discussion

This study indicates that value of pearson correlation coefficient is very strong indicating that hand length can be used to estimate height. Mean height of the students was 63.26 inches. Maximum height was 66.50 inches and minimum height was 59.40 inches. Mean RHL was 7.30 inches. Maximum RHL was 7.80 and minimum was 6.90 inches. Value of r was 0.780 and 0.752 between stature and right hand length as well as left hand length. In Maldives a study carried out resulted in a value of 0.7.[14] In India a study indicated a positive strong correlation with a 0.7 value of r.[15] In Bangladesh another study resulted in a very strong and statistically significant value of r i.e., 0.9.[16] A study carried out in Utter Pradesh on medical students value of r was found to be 0.644 & 0.598 for right and left hand length respectively.[17] Value of r was 0.78 & 0.77 between height and hand length (RHL&LHL). This study was carried out on Kashmiries.[18] Similarly in Malayshia 259 university students were studied. Value of r was found to be 0.7.[19] In Srilanka same value of r was seen in a study.[20] Value of F gives the information about the model whether it is statisticall significant or not.[21,22] In this study value of F was 216 & 181.12 indicating that both the model can be used to estimate height from hand length. Value of t is also indicative of reliability of each variable.[23]

Conclusion

Hand length can be used to estimate standing height. The regression equation can help to estimate height for identity purpose as well as for clinical treatment of a bed ridden patient.

Conflict of interest: *None*

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Authors Contribution

MA: Conceptualization of Project
MA, AK: Data Collection
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MA: Statistical Analysis
AAT, MA: Drafting, Revision
UA, AK: Writing of Manuscript

Effect of Cassia Fistula Bark Hexane Extract on Lipid Parameters in Male Diabetic Rats

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Abstract

Objective: To evaluate and compare the effects of Cassia fistula bark on serum lipids in high fat diet and streptozotocin instigated diabetic albino rats.

Method: Randomized controlled trial (RCT) carried out in Physiology department of Services Institute of Medical Sciences, Lahore from August 2017 to April 2018. Ninety male albino rats were randomly divided into two equal groups (n=45). Firstly, rats in both groups were fed on high fat diet. Secondly streptozotocin was injected to induce type 2 diabetes. The diabetic control group was designated as group-1 and kept on normal saline only. The Diabetic experimental group was fed on Cassia fistula bark (0.45g/kg body weight once a day) respectively for 30 days. Subsequently, blood samples (4-5ml intracardiac) were collected from each group member on the 31st day to evaluate the biochemical parameters of serum lipids.

Results: The hexane-based extracts of Cassia fistula lead to highly significant ($p<0.001$) reduction in lipid profile of group-2.

Conclusion: Cassia fistula bark can significantly lower serum lipid parameters.

Keywords: Cassia fistula, Lipid Lowering Effect.

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Introduction

The incidence of diabetes mellitus is predicted to increase globally from an estimated 382 million in 2013 to 592 million by 2035.[1] Type 2 diabetes has already attained epidemic level, while the incidence of type1 diabetes is also increasing. It initially emerges as a group of disorders with defective or deficient insulin secretory process culminating in glucose underutilization, hence, leading to hyperglycemia and increase mobilization of fats from adipose tissue and used as fuel instead of glucose.[2] Patients with diabetes may suffer with wide range of microvascular complications such as as stroke, ischemic heart disease especially if related with hypertension, diabetic retinopathy and nephropathy.[3] Dyslipidemia associated with diabetes typically consists of raised triglycerides, cholesterol, LDL and low HDL levels which increases the risk of coronary artery disease. Others complications include periodontitis, neural disorders, gastro-enteritis, delayed gastric emptying, renal disorders, dermatological manifestation, erectile dysfunction and diabetic macular edema.[4] Medicinal herbs have played a significant role in treating and preventing a variety of diseases worldwide for centuries. Herbal remedies are tried globally to treat diabetes mellitus proactively or to delay any further complications. They are considered a significant source of antioxidants which help in preventing or delaying many diseases and their adverse outcomes.[5] Such remedies not only seem to increase the insulin secretion and cellular glucose uptake but also decrease the intestinal glucose absorption and hepatic glucose production.[6] One of the conventional herb used to treat diabetes mellitus is Cassia fistula commonly known as amaltas. It's found in abundance

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in asian subcontinent. Many pharmacological and biological effects are attributed to various parts and extracts of this plant, including anti-diabetic, hypolipidemic, anti-inflammatory, antioxidant,[7] antiplasmodial, anti-trypanosomal, anti-cancerous, antimicrobial, anti-helminthic, anti-infertility, immunomodulating, nematicidal, immune-contraceptive and insect repellant effects.[8,9]

Therefore, The present study is the experimental type and aims to add value to future research in elaborating the protective properties of hexane extract of amaltas bark specifically on serum lipid profile. Although many researches have been carried out that uses amaltas as their subject of interest to study blood pressure, obesity, and hyperlipidemia but our study is different as we used hexane extract of amaltas bark on diabetic grounds to assess the fluctuation in lipid parameters including serum triglyceride, cholesterol, VLDL, LDL and HDL.

Materials and Methods

Randomized controlled trial (RCT) carried out in Physiology department of Services Institute of Medical Sciences, Lahore from August 2017 to April 2018 Adult and healthy male albino rats (ninety) were housed in groups of 45 per cage for minimally one-week prior to the commencement of experiment. Dwelling environment was kept at 26±2°C with 12-hour light/dark cycle. The rats were divided in two groups of 45 each. Initially all rats were given high fat diet for two weeks. On the 14th day injection streptozotocin was given to induce diabetes, confirmed by blood glucose levels > 200 mg/dl. Group 1: Diabetic control provided with normal saline orally. Group 2: Diabetic experimental was given cassia fistula extract of dose 0.45g/kg body weight for thirty days. On 31st day, intracardiac blood sample (4-5ml) was obtained to evaluate the effects of plant extract on lipid profile.[10] Freshly matured bark (5kg each) of cassia fistula were fetched locally from Lahore. Botanical identification of the bark was completed in the Botany Department, Punjab University. An 80% hexane extract of the air-dried and coarsely ground cassia bark was obtained via standardized Soxhlet extractor in Applied Chemistry Research Centre, PCSIR Labs, Lahore. The extract thus acquired, was subjected to filtration and ethanol (solvent) evaporation in a rotary evaporator in a vacuum. A dark brown concentrate, obtained post-evaporation, was then preserved at 4°C. Preceding to every dose, the crude extract was liquefied in sterilized distilled water and diluted to the required concentration.

Initial blood sample was drawn aseptically from tail vein 72-hours after streptozotocin injection to confirm hyperglycemia. Sampling was repeated on the 31st day of the experiment after ensuring the animals were fasting overnight. Each rat was anesthetized using ether before drawing 5-milliliter blood from their intracardiac sampling.[11,12] Four ml of each sample was allowed to coagulate at room temperature in the test tube for 30 minutes followed by centrifugation at 5000 rpm for 20 minutes. Post-centrifugation, the serum was collected and preserved in labeled tubes. It was kept at -20°C, to be tested for serum cholesterol, triglycerides, VLDL, LDL and HDL,. later on. PASW (formerly SPSS) was used to conduct data analysis. The student t test was carried out for descriptive analysis to find the arithmetic mean± SD values of obtained data. The values were appraised highly significant when the p-value was less than 0.001.

Results

In this randomized controlled trial, the effects of Cassia fistula (amaltas) bark on the serum lipid profile of a total of 45 male diabetic rats was evaluated. The serum cholesterol, triglyceride, LDL, and VLDL in diabetic experimental group was found to be highly significant (p=0.00) greater in both groups after inducing diabetes (Table-1). Similarly, serum HDL level was also significantly higher in both groups (Table-1). After administering amaltas bark extract, the mean difference showed a highly significant (p=0.00) drop in cholesterol, triglyceride, LDL, and VLDL levels; and highly significant (p=0.00) rise in serum HDL level in treated group compared to the untreated diabetic control group.

Table 1: *Comparison of Serum Lipid Profile between Diabetic Control and Diabetic Experimental Groups*

Parameters	Group I (n=45)	Group II (n=45)	p-value
Serum triglyceride(mg/dl)	100.82±5.30	80.53±4.62	0.00**
Serum cholesterol(mg/dl)	214.57±6.88	100.15±5.67	0.00**
Serum HDL (mg/dl)	16.57±2.82	18.06±4.09	0.05*
Serum LDL (mg/dl)	178.56±8.13	31.58±7.18	0.00**
Serum VLDL (mg/dl)	20.13±1.06	16.08±1.01	0.00**

Values are expressed as Mean ± SD
* p-value is significant
** p-value is highly significant

Discussion

Recently, more research is being focused on unveiling

the antidiabetic properties of cassia fistula in search of some harmless herbal alternative to allopathic medicines. For this purpose, meta studies are being carried out to assess the effects of various aqueous, ethanolic, methanolic and petroleum extracts from all parts of the plant on blood pressure, hyperlipidemia and obesity.[13,14]

The current study is focused to evaluate and compare the lipid lowering outcomes of hexane extract of amaltas bark in HFD-streptozotocin induced diabetic rats. When induced with high fat feeding and streptozotocin, both rat groups showed a rise in serum triglyceride, total cholesterol, VLDL, LDL levels (p=0.001). Also, serum HDL levels were lower in both groups (p=0.000). The serum triglyceride, total cholesterol, & LVDL- cholesterol reduced; and HDL-cholesterol increased in the experimental groups treated with the hexane extracts of amaltas (cassia fistula) bark versus the untreated diabetic controls. Similar results were obtained by Rizwana et al,[15] when high fat diet induced hyperlipidemia rats were treated with three different doses i.e 100, 300 and 500 mg/kg of ethanolic extract of CF fruit for 30 days and obvious hypolipidemic as well as antioxidant outcomes were seen by measuring lipid parameters include serum triglyceride, cholesterol, VLDL, LDL and HDL. Therefore, the administration of high dose of CF extract 500 mg/kg showed exceptional good results which was comparable to the effects of standard drug atorvastatin.[16,17] Meanwhile, the earlier report of Guruprasad et al, has reported that administration of aqueous and methanolic leaf extracts of C. fistula L. at 200 and 400 mg/kg b.w. reported significantly reduction in lipid parameters in rats which were fed with atherogenic diet for 21 days.[18] Hence, the results of our study indicate the potential lipid lowering benefits of using the cassia fistula in herbal medicine and warrants further research and human trials.

Conclusion

Hexane based extract of cassia fistula bark is a potent lipid lowering agent.

Conflict of Interest: *None*

Source of Funding: *None*

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Authors Contribution

NZ: Conceptualization of Project
NZ, ME, NK: Data Collection
NI: Literature Search
NZ, FA: Statistical Analysis
NZ, FA: Drafting, Revision
NZ, ZF: Writing of Manuscript

E-Learning among Medical students of Pakistan: Challenges and Opportunities

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Abstract

Objective: The study was done to assess the impact of E-learning methodologies on medical students of Pakistan.

Method: A cross-sectional study was conducted from 16th September 2021 to 16th October 2021. Research questionnaire was constructed on google-forms, and it was electronically distributed amongst the students studying in various medical colleges of Pakistan. 188 students were included in this study. The questionnaire was designed to scale the students' IT skills, their experience of previous participation in any online courses, comparison of face-to-face learning and e-learning in terms of acquiring knowledge, clinical skills, social competences and possible advantages of e-learning. Descriptive statistics were used to analyze different parameters including advantage and disadvantage of e-Learning and it's acceptability by the students. The Chi-square and Mann-Whitney test were used to compare answers. P value <0.05 was considered statistically significant.

Results: Seventy-two male and 116 female students responded to the questionnaire. Most of the participants found it less effective than in person learning in terms of increasing skills (Mean=3.67, Mean=1.68, respectively) (P<.0001). However, most of them (76.60 %), found it very convenient specially when staying in the safe environment of home was the most important need of the time as in COVID- pandemic. In that hour of the need, an opportunity to learn by e-learning was very promising. Reduced interaction with the teacher was indeed the single disadvantage highlighted by most participants (P= 0.0075). A total of 25 (13.30%) respondents rated e-learning as enjoyable. There was statistically significant difference between answers given by students in the years of studies (P=0.004).

Conclusion: The use of online teaching platforms has helped in minimizing the disruption in medical teaching caused by the Covid 19 pandemic. Integration of both e-learning and campus-based learning would be beneficial in future medical teaching allowing for more flexibility of learning.

Keywords: *e-learning, covid-19 pandemic, challenges, medical students, impact*

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Introduction

WHO declared Coronavirus Disease 2019 (COVID-19) a pandemic in March 2020. To date, millions of people have been affected.[1] The disease has not only taken a toll on the health system but the nationwide lockdowns that were implemented to contain the spread of the disease resulted in the closure of the educational institutes as well.[2]

This posed a considerable challenge for medical education, as the teachers must deliver the lecture in a safe environment while making sure that the integrity and steadiness of the medical education process are

not affected.[3] Medical schools had to suspend clinical rotations and observations in hospitals, general practice as well as community settings. This may result in the decline of clinical skills competency of the students and adversely affect their future training.[4] E-learning was therefore implemented worldwide in order to provide students with opportunities for continuous learning.[5] The common methods used for E-learning were scheduled live online video lectures with interactive discussions along with prerecorded teaching material which was provided to the students so that they can learn at their own pace.[6] The socioeconomic status of a country also plays a vital role in the educational progress of the students. Students residing in countries with high socioeconomic status are reported to have faced less difficulty in pursuing their education due to the easy accessibility of the resources[4]. However, the students residing in middle or low-socioeconomic-status countries have had difficulty in arranging electronic devices and the unavailability of a stable internet connection to a number of places has also added to the problem.[7] It is due to the same reasons that the majority of students in Pakistan have been reported to have a negative perception of online teaching methods.[8]

We undertook this study to access the impact of online teaching methodologies on medical students of Pakistan. This will help us to understand the willingness of medical students to acclimate to this new environment of online learning.

Material and Methods

A cross-sectional study was conducted from 16th September 2021 to 16th October 2021. The research questionnaire constructed on Google Forms was disseminated via online social media platforms (Facebook, WhatsApp, and Gmail) amongst the medical students at various colleges in Pakistan. The study included all undergraduate medical students studying in Pakistan. Residents as well as postgraduate students were excluded. The respondents were told about the objectives of the study, and it was voluntary participation. A total of 188 students took part in the study. The research was approved by the Institutional Review Board of CMHLMC & IOD. Items in the questionnaire were based on previous literature (Bączek M et al)[9]; some questions were modified taking into account the local conditions. The questionnaire contained four parts.

The first section was about participants 'general information. They were required to provide their age, gender, academic year, medical college, number of siblings, family's monthly income, and access to computer and internet services). In the second section of the questionnaire, the existing IT knowledge of the students was evaluated whether they have taken any online courses of any sort in the past. They were given six options regarding the benefits and shortcomings they faced during eLearning. They were able to choose as many options as they think were appropriate. The third section of the questionnaire used a Likert scale (1-extremely ineffective, 5-extremely effective) for comparison of face-to-face learning and e-learning as regards acquiring knowledge, clinical and social skills. Moreover, the students were also asked to rate their participation during classes ranging from extremely inactive to extremely active. It was scaled from 1 to 5 (1 being extremely inactive, 5 being extremely active). The Likert scale was used to mark the acceptability level of students for the online learning sessions (1-extremely unenjoyable, 5- extremely enjoyable).

The data were analyzed with (Excel - 2019, IBM SPSS Statistics 26.0, Minitab - 17, and MedCalc) statistical software. Descriptive statistics were used to evaluate the benefits, disadvantages and acceptability level of eLearning among the students. Comparison between face-to-face learning and online learning experience was done by using the nonparametric Wilcoxon signed-rank test. The Chi-square and Mann – Whitney tests were used to compare answers given by students belonging to different academic years. $P< 0.05$ was considered statistically significant.

Results

The study included 188 participants out of which 72 (38.30%) were male while 116 (61.70%) were females. All of them have an age between 17 to 27 years with a mean of 21.165 and SD=1.884. 44 students already had some experience of online learning, they comprised 23.40% of the total students. However, the majority (76.60%) had no previous eLearning experience. IT skills of 19 respondents (10.11%) were determined to be high while 127 participants showed moderate awareness and 42 (22.34%) had minimal IT skills**.** The convenience of staying at home was the most frequently selected advantage by the majority of respondents (76.60%) followed by the access to online material (52.13%), facility of access to online materials (52.13%) and

learning at their own pace (55.85%). A few of the students (8.51%) highlighted class interactivity also. The main disadvantage of e-learning was found to be reduced interaction with the teacher (P= 0.0075), and lack of self-discipline (P=0.0070). The difference between face-to-face and online learning was found statistically significant (P<.0001). These were recorded in terms of opinions about improving clinical skills and social interactions **(Table-1).** Students assessed that they were less active during online classes (Mean=3.39) compared with traditional classes (Mean=2.40)

Table 1: *Demographics of the study population (n=188)*

Demographic Characteristics	n (%)
Gender	
Male	72 (38.30 %)
Female	116 (61.70 %)
Age	
17 – 20	62 (32.97 %)
21 – 24	121 (64.36 %)
25 – 28	5 (2.65 %)
Year in medical school	
First Year	51 (27.13 %)
Second Year	17 (9.04 %)
Third Year	52 (27.66 %)
Fourth Year	44 (23.40 %)
Final Year	24 (12.77 %)
Family's Monthly Income	
[illegible]	85 (45.21 %)
Between 100,000 - 200,000	51 (27.13 %)
Between 200,000 - 400,000	31 16.49 %)
>400,000	21 (11.17 %)
Where do you live?	
Urban Settlement	125 (66.49 %)
Semi - Urban Settlement	45 (23.94 %)
Rural Settlement	18 (9.57 %)
Family Members	
3 - 6 Members	138 (73.40 %)
7 - 9 Members	44 (23.40 %)
10 - 12 Members	5 (2.66 %)
Room of you own or do you share	
Yes	76 (40.43 %)
No	112 (59.57 %)
Devices do you own?	
Smart-Phone	187 (99.47 %)
I-pad or Tablet	23 (12.23 %)
Laptop	126 (67.02 %)
Desktop Computer	17 (9.04 %)
Buy a new device?	
Yes	39 (20.74 %)
No	149 (79.26 %)
Internet access at home or currently studying?	
I don't have internet access and I have to go somewhere else	9 (4.79 %)
Prepaid mobile data	64 (34.04 %)
Postpaid internet subscription, but the connection is slow and/or unreliable	46 (24.47 %)
Postpaid internet subscription, but the connection is fast and reliable	69 (36.70 %)
IT skills	
Low	42 (22.34 %)
Moderate	127 (67.55%)
High	19 (10.11 %)
Participated in e-learning before the pandemic?	
Yes	44 (23.40 %)
No	144 (76.60 %)

Table 2: *Advantages and disadvantages of e-learning*

Advantages of e-learning?	First Year	Second Year	Third Year	Fourth Year	Final Year	P-value	n	Percentage (%)
Access to online materials	23	7	33	25	10	0.506	98	52.13%
Learning at your own pace	22	9	34	28	12	0.686	105	55.85%
Convenience of staying at home	33	12	41	38	20	0.466	144	76.60%
Classes interactivity	0	2	3	8	3	0.209	16	8.51%
Ability to record a meeting	18	3	28	18	11	0.679	78	41.49%
Comfortable surrounding	15	11	23	25	15	0.301	89	47.34%
Disadvantages of e-learning?								
Reduced interaction with the teacher	42	11	36	30	20	0.843	139	73.94%
Technical issues	37	9	39	36	19	0.128	140	74.47%
Lack of interaction with patients	30	7	40	35	19	0.653	131	69.68%
Poor learning conditions at home	34	6	23	18	10	0.826	91	48.40%
Lack of self-discipline	32	8	29	31	18	0.180	118	62.77%
Social isolation	24	8	23	20	11	0.259	86	45.74%

(P<.0001) **(Table- 2).** A large majority of students (106 i.e., 56.38 %) did not enjoy the online learning experience. For 31.92% of them, it was extremely unenjoyable. On the other hand, only 25 respondents (13.30%) found it enjoyable, among these, 12 found it extremely enjoyable while others found it somewhat enjoyable. There was a statistically significant difference between answers given by students belonging to different academic years. (P=0.004). There was no statistical difference between female and male students (P=.595).

Discussion

Quoting a famous saying by Dickens, "it was the best of times, it was the worst of times" might have been written for the covid pandemic. For those of us used to the age-old methods of conventional campus-based education, this was the worst of times. However, this was an excellent opportunity for the opening of new horizons especially distant learning with flexible options. [10] Medical colleges had a delicate task to balance the need for mentoring, face-to-face contact, and supervision which play an important role in the development of higher-order cognitive skills, in the pandemic. Use of e-Learning tools have expanded rapidly, and the use of mobile phones and online technology is getting increasingly accessible. [11] In the present study, the overall feedback of the students concluded that in terms of developing skills, face-to-face interaction was seen to be more effective than e-learning. Students considered themselves being less active during online classes (Mean=3.39) compared with traditional face to face classes (Mean=2.40). This is consistent with a study in which overall preference of students for online teaching was lower (1.69) as compared with face-to-face teaching (2.55).[7] However, in another study, 67% students were satisfied with their E-learning experience.[12] Reasons for students' preference might be the unexpected sudden introduction of online teaching, inadequate preparedness of the faculty and technical difficulties. Among the advantages of e-learning, the frequently cited benefits of e-learning chosen by the respondents was the convenience of staying in their houses (76.60 %). This is comparable to a research in which the respondents identified "time efficiency" (15.7%), "convenience" (14.7%), and "accessible" (11.6%) as the top three bene-fits of e-learning.[13] In the present study, the respondents were asked a num-ber of questions related to the pros and cons of e-learning. Besides the advantage of convenience of staying home, learning at their own pace (55.85 %), comfortable surroun-dings (47.34%) and ability to record a meeting (41.49 %) were among the other major advantages noted by the students. In a study done in Jordan in undergraduate students of Ophthalmology, the major advantages noted by 95.5% of the respondents was flexibility of e-Lear-ning to time and place.[14] Another research conducted in Pakistan which examined medical graduates' opinions of online education during the Covid19 outbreak found that the students approved of its integration into the exis-ting teaching methodologies. Although they were of the view that e learning was not flexible in learning process, but it saved time. [15] In our study, no distinction existed between the male and female respondents to the acceptance of e-learning. However, in another study, female students demonstra-ted a more positive attitude towards e learning as com-pared to male students.[16] In the present study, almost 76% of the participants had never participated in e-learning before the covid pandemic. This is understandable as the current generation never faced a calamitous pandemic of this magnitude. This is similar to another study done in Zimbabwe where 85% of the respondents had no prior experience of using any e-learning platform before the covid 19 pandemic.[17] In another study conducted in Sudan, 24 % reported that they were unfamiliar with E-learning systems.[18] In the current study, the major drawbacks cited by the students were reduced communication with the teacher, technological issues, lack of interaction with patients, poor learning conditions at home, lack of self-control and social isolation. One of the reasons for these might be the sudden start on e-learning for which the students and the teaching faculty were not ready. In another study conducted in Jordan, the most common challenge faced by the students was internet connectivity issues (33.5%), followed by the feel of anxieties (25.9%), not having a separate room to study at home (22.5%), and not having a device to attend online classes (18.1%).[14] One of the causes might be students in remote and rural places experiencing bad internet access.The present study was conducted to help understand the impact of e-learning on the medical students and their willingness to adopt to the change. More studies like this need to be carried out to have a broader picture of the online platforms and its impact on the future of students. One of the limitations in our study was the small sample size, owing to the poor response from the students in filling the questionnaire in due time.

Conclusion

The use of online teaching platforms has helped inminimizing the disruption in medical teaching caused by the Covid 19 pandemic, allowing for the delivery of uninterrupted medical education to students. This article addresses a gap in our understanding of the poten-tial of e-learning and the difficulties faced by the students and teachers to implement it.

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Authors Contribution

KHC, AA: Conceptualization of Project
KHC, MR, AA: Data Collection
KHC, FZ: Literature Search
MI, AA, BAG: Statistical Analysis
KHC, MR, AS: Drafting, Revision

Experience of Direct Observation of Procedural Skills by Postgraduate General Surgical Residents of Public and Private Sector Hospitals of Lahore

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Abstract

Objective: To evaluate the experience of DOPS in general surgical residents based on their perspective of its usefulness.

Method: This cross-sectional descriptive study was conducted over a period of two weeks among general surgery postgraduate residents (FCPS) of Lahore. Data was collected through a questionnaire having two responses. Each resident answered to one response at a time. Data was analyzed using SPSS 26.0.

Results: There were 189 residents in the sample. Most of the resident 156(82.5%) selected DOPS as useful tool of assessment while 33(17.4%) considered it not useful. In response 1 group Almost all residents 155(99.4%) considered DOPS a more practical assessment method having consensus that it helped them in improving skill and knowledge. However, Residents who disagreed DOPS improved their time management were 11(7.1%). Residents who do not have a freedom to choose a skill were 57(36.5%). Constructive feedback was not given in 26(16.7%) of residents. In response 02 group Assessor appointment was considered difficult by 32(97%) of residents. Feedback in 30(90%) residents was not given soon after DOPS. Residents who agreed that they do not have the prior orientation of DOPS were 32(97%). Most of the residents 69.9 % and 66.7% were assessed by Senior registrar of department in group 01 and group 02 respectively.

Conclusion: DOPS is a cost effective, feasible method of assessment with direct observation of trainee while performing a skill however constructive feedback should be given in time for improvement in future performance.

Keywords; DOPS (Direct Observation Procedural Skills), FCPS (Fellow of College of Physicians and Surgeons Pakistan).

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Introduction

Surgery is demanding and challenging field of medicine, many ambitious and hardworking students adopt it as a career. With all the charm there also comes the responsibility of safe clinical practice, a small mistake during a surgical procedure can lead to permanent disability to the patients. Therefore, surgical training provided to a training surgeon is of utmost importance and must meet the highest defined standards. Postgraduate residents must be trained in a standardized way to gain the clinical competence.[1] Structured training programme was first started in Germany in 1880s and then introduced by Dr William S Halsted in United states of America. He proposed the Halstedian Model of surgical training with focused on standardized surgical training by mentorship and communication skills to address the complexity of increasing surgical procedures and training of surgeons. Halstedian Model is the foundation of current modern surgical learning.[2,3]

Medical students in Pakistan after graduating from five year programme of MBBS are inducted in General

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Surgical training. College of Physicians and Surgeon of Pakistan (CPSP) enroll them in four year training programme of Fellow of College of Physicians and Surgeons (FCPS) in general surgery which comprises of supervised apprenticeship. General surgery residency is one of the most tough training for a postgraduate resident. During training the postgraduate residents are being assessed by conventional methods, MCQs, Short cases, long cases, e-log entries and intermediate module.[4]

In recent years CPSP has emphasize on conducting regular (DOPS) for formative assessment and feedback to improve the postgraduate training.[5] DOPS was first introduced by the Royal College of Surgeons (Norcini & Mckinkley 2007) as work place based assessment tool and now it's a part of assessment of doctors in specialist training. It was specifically designed to assess the procedural skills of training doctors in real time situation in a single encounter with patient where assessor rate the performance of residents and gives immediate feedback and mentions their strengths and weaknesses for further improvement, which distinguishes it from other forms of assessment tools.[6]

Several studies showed both strengths & weaknesses of DOPS and its acceptance among teachers and residents. Major weaknesses documented are related to conducting DOPS and receiving feedback from assessor. There are several prime advantages as well, it is an assessment of performance in a real situation and constructive feedback is provided at the working place of residents.[5,7] As Currently surgical practices of residents are un satisfactory and around 80% of residents do not receive productive feedback, it is very important to incorporate DOPS in surgical training of postgraduate resident for teaching of safe surgical skills through standardized assessment technique at workplace.[8]

It is need of time to develop a more standardized assessment programme to facilitate the surgical residents in Pakistan. As Minimal literature is available in Pakistan regarding DOPS and no prior local study was conducted among General Surgical residents, The Objective of this study is to evaluate the experience of DOPS in residents based on their perspective of its usefulness in assessment and improvement of procedural skills. Evidence collected through this study will be write to CPSP for further improvement in assessment of residents during training.

Material and Method

This cross sectional descriptive study was conducted over two weeks period in general surgical departments of government and private hospitals in Lahore after approval from IRB . General surgery postgraduate residents of FCPS doing training in tertiary care government and private hospital were included in study. Sampling technique was non probability, convenient . Sample size of 189 postgraduate residents is calculated by Raosoft with margin of error 5% and Confidence level 95%[4] Data collection was done using questionnaire. Pilot study was conducted on five postgraduate residents who faced no difficulty in completing it. Each registrar of surgical department within Lahore was contacted and asked to distribute the questionnaires to general surgical residents. The questionnaire was having two responses, Response 1 (DOPS as useful assessment tool) and response 2 (DOPS not useful tool for assessment), Each participant completed one response at one time. Residents rated response statements on a five-point Likert scale (1 strongly disagree to 5 strongly agree). Demographic data like gender, age, Grade of training (1^{st} year , 2^{nd} year, 3^{rd} year, 4^{th} year), Assessor Grade (Senior registrar, assistant professor, associate professor, professor, other) and number of DOPS attempted were recorded. The questionnaire was received back after completion in one week time. A follow-up call was made after one week to surgical registrar to follow non-responders. Consent and confidentiality of data was ensured. Data was entered and analysed using SPSS 26.0. Mean and standard deviation were calculated for quantitative variables. Frequency and percentage was used for qualitative variables.

Results

Participants were divided into two groups according to the response they completed. Response 01 was completed by residents who considered DOPS as useful activity. There were 12 questions for response 01. Total 156(82.2%) of residents completed it out of which 112(71.8%) were male and 44(28.2%) were female. There were 76.3% residents from government and 23.7% from private hospitals. Mean age of residents was 28.05 years. Table 01 is showing the results of response 01. Almost all residents 155(99.4%) considered DOPS a more practical assessment method and 152 (97.4%) residents thought its better than traditional assessment tools. All of the resident were having consensus that it helped them in improving skill and knowledge. However, Residents who disagreed that DOPS has improved their time management were 11(7.1%). Resi-

Table 1: *Response/Group 01:Students who considered DOPS as useful assessment tool*

	Questions	Strongly Disagree 1	Disagree 2	Neither Agree nor Disagree 3	Agree 4	Strongly Agree 5
1	It is a more practical assessment of a skill on real patient	NR	NR	1(0.6%)	97(62.2)	58(37.2%)
2	It has evaluated my Ability to perform a skill in a standardized way	NR	2(1.3%)	11(7.1%)	78(50%)	65(41.7%)
3	It improves student-teacher relationship	NR	1(0.6%)	3(1.9%)	87(55.8%)	65(41.7%)
4	It improves the Time management while performing a skill	NR	11(7.1%)	32(20.5%)	76(48.7%)	37(23.7%)
5	I have complete freedom to choose a skill for DOPS	NR	57(36.5%)	53(34%)	40(25.6)	6(3.8%)
6	It will help me to pass my final fellowship exam	NR	NR	10(6.4%)	91(58.3%)	55(35.3%)
7	It Helped me in learning and improving my skill	NR	NR	NR	88(56.4%)	68(43.6%)
8	It provides constructive feedback about my own performance and understanding	NR	26(16.7%)	45(28.8%)	67(42.9%)	18(11.5%)
9	This exercise motivates me to perform better in residency	NR		7(4.5%0	100(64.1%0	49(31.4%)
10	It improved my confidence level	NR	2(1.3%)	13(8.3%)	94(60.3%)	47(30.1%)
11	It is more effective than traditional assessment method	NR		4(2.6%)	69(44.2%)	83(53.2%)
12	It helped me to identify my strengths and weaknesses	NR	1(0.6%)	1(0.6%)	54(34.6%)	100(64.1%)

NR ; No Response

Table 2: *Response/Group 2:Residents who considered DOPS is not a useful method of Assessment*

	Questions	Strongly Disagree 1	Disagree 2	Neither Agree nor Disagree 3	Agree 4	Strongly Agree 5
1	It is not a true reflection of capability to perform a clinical skill	NR	2(6.1%)	4(12.1%)	23(69.7%)	4(12.1%)
2	It is difficult to arrange an appointment with consultant as assessor for DOPS	NR	NR	1(3%)	9(27.3%)	23(69.7%)
3	I have to spend extra time outside working hours due to busy roster	NR	3(9.1%)	2(6.1%)	14(42.4%)	14(42.4%)
4	It adversely affected my performance	NR	10(30.3%)	17(51.5%)	6(18.2%)	NR
5	Its Feedback was not given soon after completion of skill	NR	1(3%)	2(6.1%)	20(60.6%)	10(30.3%)
6	DOPS Future improvement box was not completed by assessor	NR	7(21.2%)	2(6.1%)	15(45.5%)	9(27.3%)
7	It is difficult to keep a record of DOPS	NR	NR	1(3%)	28(84.8%)	4(12.1%)
8	It was not seriously taken by assessor	NR	22(66.7%)	7(21.2%)	4(12.1%)	NR
9	It did not cover all important aspect of clinical practice	5(15.2%)	15(45.5%)	5(15.2%)	7(21.2%)	1(3%)
10	Its whole responsibility was put on resident for arranging DOPS	NR	2(6.1)	17(51.5%)	14(42.4%)	NR
11	I was not given the opportunity to put my own views	NR	NR	3(9.1%)	24(72.7%)	6(18.2%)
12	Performance depends on mental state of student at that particular time	NR	1(3%)	1(3%)	10(30.3%)	21(63.6%)
13	I had no prior orientation of it	NR	NR	1(3%)	10(30.3%)	22(66.7%)

dents who do not have a freedom to choose a skill to perform and assess by assessor were 57(36.5%). Constructive feedback was not given in 26(16.7%) of residents.

Response 02 was completed by residents who considered DOPS as not a useful tool of assessment. Response 02 was having 13 questions. Total 33(17.4%) residents completed this response. Mean age was 27.69, There were 23(69.7%) male and 10(30.3%) female. There were 28(84.8%) residents from government and 5(15.2%) from private hospitals. Table 02 is showing the results of response 02. Assessor appointment was considered difficult by 32(97%) of residents. Feedback in 30(90%) residents was not given after DOPS. Residents who agreed that they do not have the prior orientation of DOPS were 32(97%). Resident attempted only one DOPS were 29(18.6%) and 13(39.4) in group 01 and group 02 respectively. Most of the residents 69.9% and 66.7% were assessed by Senior registrar of department in group 01 and group 02 respectively .

Discussion

Traditional methods of assessment currently used by many institutes usually rely on testing just knowledge of students. Millers proposed his Pyramidal model for clinical competence with assessment of knowledge, application of knowledge, clinical skill competency, and clinical performance assessed by direct observation in real time scenario on top of pyramid. His model of competence covers all aspects of bloom taxonomy.[9] With growing interest and number of residents in surgery it become obligatory for teaching faculty to equip their students with updated knowledge and skill. Formative assessment by DOPS can be a good source to evaluate them give them timely feedback and produce safe and skilled surgeons. DOPS promotes self reflective process during assessment for acquisition of knowledge.[7,9] Now CPSP is also sensitizing supervisors to promote assessment of postgraduate residents by using work place based assessment tool like DOPS and Mini-Cex. DOPS is planned and structured in such a way that a particular skill should be performed by postgraduate resident in a standardized way according to the international guidelines.[10]

The study by Bazrafkan et al showed that DOPS can be used as effective method of assessment with 87.6% of student had acceptance of DOPS as useful method of assessment.[11] Morris et al. concluded that 70% of the participants of study labelled DOPS very useful in improvement in clinical skills.[12] Naina et al concluded that DOPS resulted in improvement of skill and confidence of residents.[13] A study By Pofanter et al shows the DOPS is an effective tool for assessment without any financial burden. In our study 82.5% of total residents have considered it as a useful and practical method of assessment which is better than traditional methods of assessment like MCQs, Short case and long case. DOPS has positive effect in building their confidence and overall improvement in their practical skill performance. In a Study by P. Inamdar et al Assessor it was proposed that both assessor and resident should be present simultaneously for assessment of a skill so that constructive feedback can be given immediately after completion of task however , long duty hours of residents and busy schedule of consultants due to prolong operation lists and different working stations may hinder this process.[14] In our study many resident had difficulty in time management and arranging an appointment with consultant for assessment of skill (DOPS). As DOPS includes examination of patient, taking consent, performing a skill for which there should be ample allocated time to complete the process. Residents inevitably needs adequate time which may be difficult in operation theatre while performing surgeries on different patients during a hectic day.[15] In our study the residents who considered it as a useful activity 16.7% disagree and 28.8% remained neutral that constructive feedback led to improvement in skill. Resident who selected (DOPS) as not a useful tool 90.9% stated the delay in feedback after task and 72.8% also mentioned that improvement box was not filled by the assessor which means either the assessors were not being trained or they were occupied in multiple tasks while evaluating the residents during a busy schedule. Many of the residents 97% from this group also found it difficult to find appointment with assessor.

The strength of this study is that it is one of the first study conducted in Lahore among general surgical residents. Their experience of DOPS in perspective of its productivity as a useful tool was evaluated by knowing the reasons. Limitations of this study are smaller sample size limited to general surgical residents of Lahore. We have only collected experience of residents in this study, For better implication of DOPS as a part of regular assessment process assessor experience is also very important.

Conclusion

DOPS is a cost effective, feasible method of assessment

with direct observation of trainee while performing a skill and constructive feedback should be given in time for improvement in future skill performance. To make DOPS more useful for postgraduate residents, area of weakness should be addressed by supervisor, as this study clearly identifies the response of residents towards it. Availability of assessors and immediate constructive feedback are essence of DOPS. Schedule and availability of assessor should be maintained in accordance with timing of student assessment roster. Residents should have prior orientation of it so that they are knowing how to participate in assessment and improvement in performance of skill to provide optimal surgical care to their patients under supervision of their mentors.

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Authors Contribution

PMR: Conceptualization of Project
MTQ: Data Collection
MZT: Literature Search
PMR: Statistical Analysis
MTQ: Drafting, Revision
MZT: Writing of Manuscript

Mean Gestational Age at Delivery in Females Presenting with Intrahepatic Cholestasis

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Abstract

Objective: To determine the mean gestational age at the time of delivery with intrahepatic cholestasis presenting in active labor for delivery in females at Shalamar Hospital Lahore.

Method: It was the cross sectional study that was conducted at Obs. & Gynae department, Shalamar Hospital Lahore with time span of 06 months. Sample Size of 140 women included in study subsequently fulfilling the inclusion criteria and all the women delivered by researcher by herself. Gestational age was noted and data analysis was done at SPSS version 17.0. Stratified groups compared by using independent sample t-test.

Results: The average maternal age at delivery time was 27.7±6.3 with a range of 18 to 40 years. Mean gestational age was 37.8±1.2 weeks. There were 84 patients (60%) were between para 0 -2 and 56 patients (40%) were between para 3-4. Mean BMI was 30.6±3.0 kg/m2. Stratification with respect to age, BMI and parity was also carried out.

Conclusion: In conclusion, in this cross- sectional study of intrahepatic cholestasis of pregnancy patients, mean gestational age at delivery was found to be 37.8±1.2 which revealed that ICP is not a risk factor for pre-term delivery.

Keywords: Intrahepatic cholestasis, Mean gestational age, Active labour.

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Introduction

Intrahepatic cholestasis during pregnancy (ICP), is a liver disorder occurred particularly during pregnancy. It is characterized as maternal pruritus during 3rd trimester, elevated bile acids in blood and higher rates of adverse pregnancy outcomes. It has significant fetal consequences.[1-3] Bile acid helps in excretion, absorption, and transport of sterol and fats in the gut & Liver. Primary bile acid, cholic acid and chenodeoxy cholic acid are structurally similar expect for one hydroxyl group at position seven. They are formed from cholesterol in the hepatocyte. Because of the toxic nature of bile acids their concentration is tightly regulated by hepatocyte. In ICP there is imbalance between secretion and excretion of bile acid within the liver.

There are many other diseases or conditions that can cause cholestasis like primary billary cirrhosis, primary sclerosing cholangitis, sepsis, viral infections like EBV, CMV, Herpes, certain drugs and alcohol. ICP is more prevalent in south Asian (0.8-1.46)% and South American (9.2-15.6)% Population. The cause of ICP comprises of genomic and ecological aspects. There are certain risk factors those increase the risk of ICP like advanced maternal age more than 35 years, multiparity, multiple pregnancy, previous history of ICP, history of use of oral contraceptive pills. The recurrence rate is about 40-60 percent. Increase in bile acids levels in blood of both; mother and her fetus, is the main element of pathophysiology, initiate itching to mother and high obstetrics complications also including mortality. Raised levels of bile acids in blood of pregnant

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female are indicative of ICP.[4] ICP can cause higher risk of preterm delivery (19-60%), meconium staining (27%), bradycardia to fetus (14%), fetal respiratory distress (22-41%), and pregnancy loss including fetal death (0.4-4.1%), especially in cases with the raised bile acid levels >40µmol/L.[5] Although exact mechanism of poor fetal outcome is not clarified yet but increase flow of bile acid from mother to fetus and reduced capacity of fetal liver to eliminate excess of bile acid is the main mechanism which leads to excessive accumulation of bile acids in fetal body effecting many organs mainly causing cardio toxicity, arrhythmia and sudden death. Accumulation of bile acid in umbilical cord can cause vasoconstriction leading to meconium staining. Increase bile acid can cause myometrial contraction by increasing oxytocin bio activity and increase release of prostaglandins. Various medications like antihistamine are used but they can only relive symptoms but not decrease the bile acid level. A naturally occurring hydrophilic bile acid known as ursodeoxycholic acid helps in deceasing bile acid level. The gestational age of females having Intrahepatic Cholestasis of Pregnancy, at the time of delivery, differs. One study showed that the average gestational age at delivery among females having ICP was 37.5±1.6 weeks.[3]One more study-also showed that the average gestational age on time of delivery in females with ICP was 37±1.2weeks.[1] but one study reported that the mean gestational age at time of delivery in females with ICP was 33.1±3.78 weeks.[6] The basic purpose of this research and study is to evaluate the mean gestational age on time of delivery in females with ICP presenting in active labor for delivery. Literature is evident that the pregnant females with ICP usually deliver after term (>37weeks). But controversial evidence has been found in literature. So, through this study was aimed to confirm that whether these females deliver at term or at preterm weeks. Because the complications of ICP as well as impact of preterm delivery is very significant for neonate especially in our part of world where the neonatal care unit services are compromised. So, obstetricians need some intervention to prevent the preterm deliveries and its consquences. But first we need to know the gestational age at time of delivery in ICP cases. This study will help us to improve our practice and update guidelines to plan strategies to reduce the burden of ICP and its associated complications.

Materials and Methods

Study Design was Cross Sectional and settings was Department of Obs. & Gynae Shalimar Hospital Lahore. Duration was six months and sample size was Sample size consisted of 140 cases was calculated by 95% confidence level, d=0.80 and taking magnitude of mean gestational age at delivery i.e. 37.5±1.6 weeks in females with ICP presenting for delivery. (n=140), sample Technique was Consecutive sampling, Non- probability. Sample selection was in sample selection below discussed criteria is used. Inclusion criteria was patients presenting with ICP as evidenced by symptom of pruritis, deranged (AST>40IU, ALT > 40IU and raised bile acids >10umol/L in active labor with age range 18-40 years with parity <5[1-3]. Exclusion criteria was multiple pregnancy (on ultrasound) Previous cesarean delivery (on history). Females with systemic problems i.e. Hypertension (HTN), (Blood Pressure >140/90mmHg), Diabetes Mellitus (Blood Sugar Random (BSR)>186mg/dl), renal problem (creatinine>1.2mg/dI), anemia (Hb<10g/d1) or liver disease before and during conception of pregnancy (AST>40IU, ALT)-401U), viral hepatitis and fatty liver. Study Tool: Data/information was gathered by filling the Performa. Subsequently obtaining approval from ethical committee of hospital 140 cases satisfying selection criteria were selected from labour room of Obs. and Gynae Department, Shalamar Hospital Lahore. Informed consent was also taken from the patients. Demographic information (name, Parity, age, and BMI) was also noted. All women were delivered by researcher herself. Gestational age was noted. Patient's distribution data is given below in the **Table-1**

Data analysis: data were entered and examined in SPSS version. Quantitative data like BMI, age and gestational age was given as standard deviation and mean. Parity was given in frequency and percentage. Stratification of data was done against age, BMI and Parity. Stratified groups compared by using independent sample t-test. P value ≤0.05 were observed significant.

Table 1: *Patients data summary.*

Distribution of Patients	Mean	Total No of Patients=140	Percentage
Age	18-30	97	69.3
	31-40	43	30.7
Gestational Age (week)	< 37	23	16.4
	≥ 37	117	83.6
Para	0-2	84	60.0
	3-4	56	40.0
BMI (kg/m2)	<25	3	02.1
	>25	137	97.9
Jaundice		21	15
Pruritus		126	90.0

Table 2: *Patients Lab test investigation*

Liver Function Test	Reference Range	Mean	Standard Deviation
ALT (U/L)	1-30	115	25
AST (U/L)	1-21	88	23
Total Billi Rubin (mg/dl)	0.22-1.2	3.5	1.8
Bile Acid (µmol/L)	6-7	30	4.5

Results

Total 140 females were taken in this study during the period of 06 months. The average maternal age at time of delivery was 27.7±6.3 with a range of 18 to 40 years. Mean gestational age was 37.6±1.2 weeks. There were 84 patients (60%) were between para 0-2 and 56 patients (40%) were between para 3-4. Mean BMI was 30.6±3.0 kg/m2. Stratification was carried out according to age, BMI and parity.

Table 3: *Stratification for age*

Age	Gestational Age (week)	
	Mean	Standard deviation
18-30	37.69	1.27
31-40	37.64	1.34
t value	0.208	
p value	P = 0.835	

Table 4: *Stratification for parity*

Para	Gestational Age (week)	
	Mean	Standard deviation
0-2	37.67	1.30
3-4	37.68	1.28
t value	- 0.027	
p value	P = 0.979	

Table 6: *Stratification for BMI*

BMI (kg/m^2)	Gestational Age (week)	
	Mean	Standard deviation
⩽25	38.33	1.15
> 25	37.66	1.29
t value	0.625	
p value	P = 0.533	

Discussion

ICP (Intrahepatic cholestasis of pregnancy) probably affects about 1% pregnancies. In worldwide ICP is considered as the most common intrahepatic cholestatic condition.[20] During Pregnancy the respective liver capacity to metabolize pregnancy-related steroids is the most considerable contributing factors. The exact and precise etiology has still remained unidentified. It is usually seen that ICP occurs in families that suggested its genetic susceptibility. This effect also raised an interest in molecular genetic cause of ICP. ICP usually benign to mother but there are certain risk to fetus including increased risk of meconium staining, pre term delivery, fetal distress and intrauterine fetal demise. Patient with ICP in previous pregnancy should have extra surveillance in pregnancy which will reduce 80% of complications related to ICP in current pregnancy in case of recurrence. In a study by Rook et al (1) found that 33% of cases has complications related to ICP like RDS, Meconium staining, fetal distress but there was no case of intrauterine fetal demise. One other study reported 24% compilation related to ICP.[21] RDS was observed 52% of the complication which shows that RDS incidence in neonates born to ICP mother is twice of the normal population. This may be due to delivery at earlier gestation but it has been hypothesized that bile acid can cause depletion of surfactant in the alveoli. The mean gestational age in patients with history of ICP was 37 (Range 36-39) and in those without ICP was also 37 (Range 33-40). The proportion of deliveries with gestational age more than 37 weeks was 35% in patient with history of ICP and 26% in patient without ICP. In present study, mean gestational age was found to be 37.6±1.2 weeks which is comparable with the study of Rook et al (37.0±1.2) and Geenes et al (37.5±1.6.)

Conclusion

In conclusion, in this cross-sectional study of

intrahepatic cholestasis of pregnancy patients, mean gestational age at delivery was found to be 37.6±1.2 which revealed that ICP is not a risk factor for pre-term delivery.

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Authors Contribution

SR, MU, SF, ST: Conception of study, Experimentation/Study con-duction, data collection, Analysis, Discussion, Manu-script Writing RS: Critical Review Facilitation and Material Analysis Literature search, conceptualization of the study, Interpretation, Proof study and review.

Diagnostic Value of Total and Differential Leukocyte Counts for the Diagnosis of Acute Appendicitis

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Abstract

Objective: To establish the predictive value of total and differential leukocyte counts for the acute appendicitis diagnosis.

Method: This cross-sectional study lasted for 6 months over 95 patients. In order to determine TLC and DLC, a blood sample was taken. The patients were categorized as TLC positive or negative & DLC positive or negative. Appendectomy was performed to determine whether the patient was positive or negative. TLC and DLC's sensitivity, specificity, PPV, NPV, and diagnostic accuracy were calculated & outcomes mentioned.

Results: Patients had mean age of 31.20±12.14 years. A total of 60 women (63.2%) and 35 men (36.8%). Patients' mean body mass index was 23.394.87kg/m2. We calculated a mean time to resolution of 6.603.53 hours. TLC averaged 13413.12 ±8142.58 per milliliter. Overall, the DLC averaged 76.33 ±12.56%. TLC had a Sensitivity of 90.7%, Specificity of 96.2%, PPV of 95.1%, NPV of 92.6%, and Diagnostic Accuracy of 93.7% to diagnose acute appendicitis. For DLC, Diagnostic accuracy was 88.4%, sensitivity 88.4%, specificity 76.9%, PPV 76%, NPV 88.9% & PPV of 76% for identifying acute appendicitis.

Conclusion: In an emergency setting both TLC and DLC were reliable enough allowing the patients to have some confirmation that they were experiencing the signs of acute appendicitis and avoiding an appendectomy or unneeded surgery in at least the negative cases.

Keywords: Appendectomy, Acute appendicitis, Differential leukocyte count, Total leukocyte count, Histopathology

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Introduction

Acute Appendicitis is one of the most common cause of sudden stomach pain. Patients presenting with typical symptoms may have a straightforward clinical diagnosis, but those with less common presentations may face diagnostic uncertainty and treatment delays.[1] Forty-eight percent of patients with classic symptoms of acute appendicitis were indeed suffering from the illness.[2]

When diagnosed with acute appendicitis, abdominal pain is typically the patient's first symptom. One may have mild to severe nausea, vomiting, and loss of appetite. Following localization of the discomfort to the right iliac fossa, an examination reveals localized tenderness of the abdomen and muscular rigidity.[3] Elevated leukocytosis with a left shift is typically seen in lab results upon initial presentation.[4,5]

The evaluation of a patient presenting to the emergency department with significant abdominal discomfort can be challenging. Poor patient outcomes can result from

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incorrect diagnosis, which can be delayed or prevented by a muddled presentation caused by a number of reasons. Clinicians need to take into account the possibility of multiple diagnoses, especially in the case of serious illnesses that call for immediate treatment to reduce the risk of serious complications or death.[6,7]

Diagnosing acute appendicitis can be aided by a total leukocyte count (TLC). Patients with acute, uncomplicated appendicitis typically have a white blood cell count (WBC) more than 11,000/ml and they also typically have a moderate polymorphonuclear predominance.[8,9] One further test that can aid in diagnosis is the differential leukocyte count (DLC). The neutrophil count is a primary indicator of DLC, and a value of > 80% indicates an issue.[10,11] To diagnose acute appendicitis sensitivity of TLC is reported to be 86.9% and a specificity of 81.25%, while the sensitivity of DLC is 82%, with a specificity of 68.75%.[10] That they can both be utilized to anticipate acute appendicitis is demonstrated. However, other research indicates sensitivity and specificity of TLC to be 64.8% and 89.4% for diagnosing acute appendicitis.[12] The aim of our study is to establish whether TLC or DLC is more accurate in predicting acute appendicitis when using appendicitis as the gold standard. TLC and DLC have been shown to be effective in determining whether a patient's stomach pain is actually related to acute appendicitis, hence preventing unnecessary operations. However, different findings have been reported in the literature.

There was some discrepancy between the studies on TLC's accuracy compared to DLC. As limited local data is available, this study was designed to determine that whether TLC is sufficient for diagnosis of acute appendicitis or if further interventions are required? In the future, we can adopt TLC/DLC count-based screening for patients complaining of stomach pain before deciding whether to send them to the operating room. The findings of this research will reduce the workload of surgeons and hospitals by reducing the number of unnecessary surgical procedures.

Material and Methods

The study's primary aim was to evaluate the predictive accuracy of total and differential leukocyte counts for diagnosing acute appendicitis using appendectomy itself as the gold standard. The information was collected using a cross-sectional validation study design in the West surgical ward, Mayo Hospital in Lahore. Six months were devoted to the investigation, beginning on November 26, 2018, and ending on May 26, 2019. The sample size of 95 cases is computed using a 95% confidence level, an expected percentage of acute appendicitis of 48%, the sensitivity of TLC of 86.9% with a 10% margin of error, and the specificity of TLC of 81.25% with a 12% margin of error, with appendectomy as the gold standard.

All those patients ranging in age from 16 to 60 years old, and exhibiting symptoms such as loss of appetite, nausea, or vomiting, as well as pain localizing to the right lower quadrant and increasing in intensity prior to appendectomy, make up the sample. Patients with a history of diabetes mellitus (BSR>186mg/dl), those who are taking non-steroidal anti-inflammatory or immuno-suppressive medicines within 2 weeks prior surgery, and patients with a perforated appendix (based on clinical examination and ultrasound) were not included in the sample. Patients included in this study were enrolled through the emergency room of surgery at Mayo Hospital in Lahore. The subject has given their informed consent in writing. Names, ages, genders, and symptom durations were collected as a means of establishing context. A 3cc disposable syringe was used to draw blood in CBC vial. Both TLC and DLC analysis were performed on all samples at the hospital's laboratory. Consulting surgeon, aided by a researcher, performed an appendectomy on all of the patients under General Anesthesia. Patient results were either favorable or negative. The data collection was followed by its entry into SPSS 21. Age, body mass index, symptoms' duration, symptom severity & TLC and DLC were just some of the quantitative factors that were shown as means and standard deviations. In this study, we used frequency and percentage displays to show gender differences in acute appendicitis (on TLC, DLC of appendectomy). Using appendectomy as the gold standard, 2×2 tables were created to determine the sensitivity, specificity, PPV, NPV, and diagnostic accuracy of TLC and DLC. The data was divided into groups based on age, gender, body mass index, and length of time they had been experiencing symptoms.

Results

In this cross sectional validation study, there were 35 (36.8%) males while 60 (63.2%) females.

With a mean age of 31.20±12.14 years, with a mean BMI of 23.39±4.87kg/m^2. The mean duration of symptoms was 6.60±3.53hours. The mean TLC was 13413.12±

8142.58 per ml. The mean DLC was 76.33±12.56%. Acute appendicitis was positive in 41 (43.2%) cases on TLC while 50 (52.6%) were positive on DLC and 50 (52.6%) were positive histopathology. For diagnosis of acute appendicitis, TLC showed Sensitivity of 90.7%, Specificity of 96.2%, PPV of 95.1%, NPV of 92.6% and diagnostic accuracy of 93.7%. Similarly, for diagnosis of acute appendicitis, DLC showed Sensitivity of 88.4%, Specificity of 76.9%, PPV of 76%, NPV of 88.9% and diagnostic accuracy of 82.1%. For the results of TLC, stratification of data done for the patients age. Patients aged 16-40 years, the sensitivity, specificity, PPV, NPV and diagnostic accuracy of TLC were 88.9%, 97.5%, 97%, 90.7%, 93.4%, respectively. In patients aged 41-60 years, the sensitivity, specificity, PPV, NPV and diagnostic accuracy of TLC were 100%, 91.7%, 87.5%, 100%, 94.7%, respectively. Stratification of data done for the patient's gender. In male patients, the sensitivity, specificity, PPV, NPV and diagnostic accuracy of TLC were 80%, 93.3%, 94.1%, 77.8%, 85.7%, respectively. In female patients, the sensitivity, specificity, PPV, NPV and diagnostic accuracy of TLC were 100%, 97.3%, 95.8%, 100%, 98.3%, respectively. Stratification of data done for the patients BMI. In underweight to normal BMI patients, the sensitivity, specificity, PPV, NPV and diagnostic accuracy of TLC were 91.7%, 100%, 100%, 95.4%, 96.9%, respectively. In overweight and obese patients, the sensitivity, specificity, PPV, NPV and diagnostic accuracy of TLC were 89.5%, 81.8%, 89.5%, 81.8%, 86.7%, respectively. Data was stratified for duration of symptoms. In patients presented within 1-6 hours of symptoms, the sensitivity, specificity, PPV, NPV and diagnostic accuracy of TLC were 86.4%, 100%, 100%, 90%, 93.9%, respectively. In patients presented after 7-12hours of symptoms, the sensitivity, specificity, PPV, NPV and diagnostic accuracy of TLC were 95.2%, 92%, 90.9%, 95.8%, 93.5%, respectively. For the results of DLC, Stratification of data done for the patients age. In patients aged 16-40years, the sensitivity, specificity, PPV, NPV and diagnostic accuracy of DLC were 88.9%, 72.5%, 74.4%, 87.9%, 80.3%, respectively. In patients aged 41-60years, the sensitivity, specificity, PPV, NPV and diagnostic accuracy of DLC were 85.7%, 91.7%, 85.7%, 91.7%, 89.5%, respectively. Stratification of data done for the patients' gender. In male patients, the sensitivity, specificity, PPV, NPV and diagnostic accuracy of DLC were 90%, 86.7%, 90%, 86.7%, 88.6%, respectively. In female patients, the sensitivity, specificity, PPV, NPV and diagnostic accuracy of DLC were 87%, 73%, 66.7%, 90%, 78.3%, respectively. Stratification of data done for the patients' BMI. In underweight to normal BMI patients, the sensitivity, specificity, PPV, NPV and diagnostic accuracy of DLC were 95.8%, 82.9%, 76.7%, 97.1%, 87.7%, respectively. In overweight and obese patients, the sensitivity, specificity, PPV, NPV and diagnostic accuracy of DLC were 79%, 54.6%, 75%, 60%, 70%, respectively. Data was stratified for duration of symptoms. In patients presented within 1-6 hours of symptoms, the sensitivity, specificity, PPV, NPV and diagnostic accuracy of DLC were 86.4%, 74.1%, 73.1%, 87%, 79.6%, respectively. In patients presented after 7-12 hours of symptoms, the sensitivity, specificity, PPV,

Table 1: *Descriptive Statistics of age, BMI, duration of symptoms, TLC, DLC of patients (n=95)*

Age (years)	**n**	**95**
	Mean	31.20
	Standard deviation	12.14
	Minimum	16
	Maximum	60
BMI (kg/m^2)	n	95
	Mean	23.39
	Standard deviation	4.87
	Minimum	16.50
	Maximum	34.87
Duration (hours)	n	95
	Mean	6.60
	Standard deviation	3.53
	Minimum	1
	Maximum	12
TLC (per ml)	n	95
	Mean	13413.12
	Standard deviation	8142.58
	Minimum	4582
	Maximum	29891
DLC (%)	n	95
	Mean	76.33
	Standard deviation	12.56
	Minimum	51
	Maximum	95

Table 2: *Distribution of Acute Appendicitis on TLC, DLC and Histopathology (n=95)*

Acute appendicitis on		Frequency	Percentage
TLC	Positive	41	43.2
	Negative	54	56.8
DLC	Positive	50	52.6
	Negative	45	47.4
Histopathology	Positive	50	52.6
	Negative	45	47.4

Table 3: *Diagnostic Accuracy of TLC & DLC against histopathology*

A: Diagnostic Accuracy of TLC against histopathology				
		Histopathology		Total
		Positive	Negative	
TLC	Positive	39	2	41
	Negative	4	50	54
Total		43	52	95
Sensitivity = 90.7%; Specificity = 96.2%; PPV = 95.1%; NPV = 92.6%; Diagnostic accuracy = 93.7%				
B: Diagnostic accuracy of DLC against histopathology				
		Histopathology		Total
		Positive	Negative	
DLC	Positive	38	12	50
	Negative	5	40	45
Total		43	52	95
Sensitivity = 88.4%; Specificity = 76.9%; PPV = 76.0%; NPV = 88.9%; Diagnostic accuracy = 82.1%				

NPV and diagnostic accuracy of DLC were 90.5%, 80%, 79.2%, 90.9%, 84.8%, respectively.

Discussion

Despite advances in surgical technology, appendicitis remains a frequent surgical emergency. Although most instances will show with classic symptoms, appendicitis can be tricky to diagnose based on physical examination alone due to the appendix's movable location.[13,14] The definitive diagnosis of appendicitis continues to be a clinical judgment, supplemented by relevant diagnostics, despite advancements in imaging modalities.[14,15] A negative result from a test cannot rule out a diagnosis if the patient's detailed history & physical examination advocate a high likelihood of a condition. Even in the presence of a life-threatening infection, like appendicitis or cholecystitis, the TLC may be normal.[16] The mean age of 31.2±12.14 years was included in our study. Out of a total of 95 participants, 60 (63.2%) were women, and 35 (36.6%) were men. In our research, more women participated than men. Within 12 hours of experiencing symptoms, patients sought medical attention. TLC had a sensitivity of 90.7%, specificity of 96.2%, positive predictive value (PPV) of 95.1%, negative predictive value (NPV) of 92.6%, and diagnostic accuracy of 93.7% when used to diagnose acute appendicitis. The diagnostic accuracy of DLC was 82.1% for the identification of acute appendicitis, with a sensitivity of 88.4%, specificity of 76.9%, positive predictive value (PPV) of 76%, negative predictive value (NPV) of 88.9%, and Diagnostic accuracy of 82.1%. Our research showed that TLC was more reliable than previous studies, including a series that found an elevated TLC of more then 11,500/mm^3 was found in 49% of 354 individuals.[17] Although a rise in TLC is indicative of the disease but still not diagnostic due to its limited specificity, hence high TLC count does not contribute more in patient care when combined with other, more conclusive clinical findings.[18] The diagnostic accuracy of a total leucocyte count was 76.5% and 73.7% in a series of 20 acute appendicitis patients, respectively. Thus, while high white blood cells in the smear raise the sensitivity for diagnosing acute appendicitis but it is not very specific and offers little in the way of diagnostic utility. Another study stated that WBCs can be normal despite having a perforated appendicitis.[17] Many studies have demonstrated that DLC can improve diagnosis accuracy. However, DLC is not as specific as other tests despite its high sensitivity. TLC with a sensitivity of 86.9% and a specificity of 81.25 % for the diagnosis of acute appendicitis, while DLC scores just 82% and 68.75 % in these categories. In this way, it helps in demonstrating their usefulness in predicting the condition, acute appendicitis. However, research shows that TLC has 64.8% of sensitivity and 89.4% of specificity for diagnosing the acute appendicitis.[12]

Conclusion

Thus, TLC and DLC were found to be reliable enough to be used in an emergency setting, allowing patients to have some confirmation as to whether or not their symptoms are indicative of acute appendicitis and thereby reducing the likelihood that patients who do not have the condition will undergo an appendectomy or other unnecessary surgeries. In this regard, we have just discovered that TLC is more reliable than DLC. However, we urge larger-scale trials to corroborate the evidence.

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Authors Contribution

JA: Conceptualization of Project
HSA: Data Collection
HJAR, MKJ: Literature Search
HJAR: Statistical Analysis
HSA: Drafting, Revision
FH: Writing of Manuscript

Role Of Pre-cesarean Section Amoxicillin with Ceftriaxone in Ameliorating Post-cesarean Infection: A Comparative Study

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Abstract

Objective: The objective of study was to assess whether preoperative administration of two broad-spectrum antibiotics (Amoxicillin vs Ceftriaxone) used a preventive measure against the maternal wound infection after CS are equally efficient against wound infection. Caesarean sections (CS) and surgical vaginal births are established risk factors for maternal infection. Surgical site infections (SSIs) happens to be a common entity and can be avoided with the use of appropriate antibiotic prophylaxis which can be given in pre/intra/post-operative period. Despite available guidelines on preoperative antibiotics prophylaxis, there are obstetricians' preferences in antibiotic selection in clinical practice. There is insufficient evidence to support the use of selective prophylaxis as current WHO recommendations do not endorse such antibiotic prophylaxis for women having uncomplicated surgical vaginal births.

Method: The study lasted for six months and was conducted in the Department of Obstetrics & Gynecology, Lady Atchison Hospital, Lahore. This comparative study was conducted with 482 subjects (aged ⩾ 16 years) from single centered tertiary care hospital, in Lahore. Women were randomly allocated into two groups; each group contain 241 participants; Group 1: was given amoxicillin before and after CS; Group 2: was given ceftriaxone before and after CS. The primary outcome of the treatment was the presence/absence of maternal infection.

Results: In the amoxicillin-received group (n=241), only 4 (1.7%) female got wound infections compared to 6 (2.5%) women of the ceftriaxone-treated group (n=241) (OR=0.751, 95% CI=0.209-2.695, p-value= 0.659).

Conclusion: In low-resource settings, a simple dosage of prophylactic amoxicillin or ceftriaxone have the same efficacy and effectiveness for preventing post-caesarean wound infections therefore both can be considered an effective prophylactic to reduce the risk of post-caesarean wound infection in the local population.

Keywords: Caesarean section, ceftriaxone, wound infection, surgical site infection, amoxicillin

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Introduction

The frequency of caesarean sections has been increasing in the last decades, both in the USA and the Asia-Pacific region.[1,2] A substantial cause of maternal morbidity and probable fatality is infections and their related complications following obstetric surgery. Caesarean delivery is the only primary risk factor for postpartum maternal infection. Women having caesarean deliveries have a five to twentyfold increased risk of infection and infectious morbidity as compared to vaginal births.[3] Generally, 70% of the total women cases with maternal mortality have severe sepsis, infection, and low survival rate with long-term health issues.[4] About 11% of maternal mortality worldwide is because of severe sepsis and infections.[5] However, 20,000 mortality cases because of pregnancy-related infections have been reported annually.[6] The pregnancy-related infection

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mortality varies globally and is reported higher in most low-income countries than in developed countries. Only USA and other nations have maternal mortality of 13% - 05% respectively.[7] A WHO global study and awareness campaign is focusing on undertreated and under-recognized maternal infection-based mortality.[8]

To lower the rate of post-caesarean surgical site infections (SSIs), surgical patients, particularly caesarean patients, have been recommended for use of proper surgical antibiotic prophylaxis as part of SSI prevention bundles.[9] Due to concerns that earlier administration of antibiotic prophylaxis for caesarean delivery would expose fetuses through the placenta, this practice has typically been performed after clamping the umbilical cord.[10] Maternal sepsis-causing risk factors may be identified from Caesarean section and operative vaginal. According to estimates, up to 16% of women who give birth via surgical vaginal delivery and 20–25% of women who give birth via caesarean section both get an infection without prophylaxis. Meta-analysis has revealed that the chances of endometritis, wound and maternal infections may be reduced by about 60-70% subject to the administration of prophylaxis.

The prophylaxis may be administrated an hour before the incision to ensure the availability of optimized concentration in the blood and tissue.[11,12] Intraoperative redosing is suggested when the antibiotic has more than two half-lives since the initial dosage of prophylaxis was administered because the probability of SSIs increased subjected to redosing during a lengthy procedure. Additionally, substantial perioperative bleeding required redosing during surgery.[12,13] Obese patients may require increased concentration for the availability of the optimum concentration of drug in tissue.[14] Despite the existence of defined standards for preoperative antibiotic prophylaxis, there are still variations in clinical procedures depending on the choice of obstetricians. Taking into account the importance of prophylaxis, the present study was planned to examine and compare the efficacy of two important antibiotics (amoxicillin, ceftriaxone) administration before caesarian section in avoiding post-operative wound infection and related complications.

Material and Method

The study lasted for six months and was conducted in the Department of Obstetrics & Gynecology, Lady Atchison Hospital, Lahore. The study was dully approved by from Ethical review board of the institute in accordance with the declaration of Helsinki. Before the enrolment, each participant was informed about the study, and consent was taken from each participant. A sample size of 482 was calculated with 80% power of the test, 90% confidence interval (CI), and taking an expected percentage of wound infection as 1% with amoxicillin and 4.8% with ceftriaxone.[15,16] Patients with ages ranging 18-40 years with parity <5 undergoing elective caesarean section (due to previous C-section, short stature, cephalopelvic disproportion (on ultrasound) were included while patients presented with gestational/chronic diabetes (BSR>186mg/dl), hypertension (BP ≥ 140/90mmHg), Anemic (Hb ≤ 10mg/dl), INR >2, PT 20sec and APTT >15sec were excluded from the study. All the participants were physically examined for Body mass index (BMI) at the time of admision. The participants were divided into two groups labeled as amoxicillin-treated and ceftriaxone treated. Each participant in each represented group was administrated with 1 gm intravenously respected dose i.e. amoxicillin or ceftriaxone after cord clamping and repeated for three days after 1st dosage followed by oral administration of tablets (amoxicillin 250mg/ cefuroxime 250mg) 6 hourly for four days. After the performance of caesarean sections, all the subjects were kept under observation for 10 days until the removal of the suture followed by an assessment of wound inspection for the presence of infection. All statistical analyzes were performed using Statistical Package for the Social Sciences (SPSS) version. 21 (SPSS Inc. Chicago, IL). Mean, the standard deviation was used for demographic parameters while the Chi-square test was used to estimate the risk of wound infection in both groups with parameters maternal age, gestational age, parity, and BMI followed by posthoc sub-group analysis. Odds ratio (OR), 95% Confidence Interval (CI) was used with a level of significance less than 0.05.

Results

A total of 482 females with a mean age of 29.56±6.62 years were recruited. The demographics and clinical information were collected and are presented in (Table-1).

The mean age of amoxicillin treated group was 29.44± 6.53 while the mean age for ceftriaxone was 29.61 ± 6.75 years (Figure 1A). The gestational age at the time of CS was 37 weeks for n=125 and 38 weeks for n=116 cases for amoxicillin treated group while n=112 and n=129 cases for ceftriaxone treated group respectively (Fig-1B). The majority of the patients had normal Basal metabolic index (BMI) and half of the patients in both groups were primigravida. Both group cases n=237

(98.3%) and n=235 (97.5%) for amoxicillin and ceftriaxone respectively showed resistance toward post-operative wound infection.

Table 1: *Demographics and Clinical information of studied subjects (n=482)*

Demographics	Amoxicillin Treated group (n=241)	Ceftriaxone Treated group (n=241)
Maternal Age (years)	29.44±6.53	29.61 ±6.75
18-30	127 (52.7%)	129 (53.5%)
31-40	114 (47.3%)	112 (46.5%)
Gestational age (weeks) At randomization		
36-37	125 (51.9%)	112 (46.5%)
37-38	116 (48.1%)	129 (53.5%)
Body Mass Index (BMI) kg/m2		
18-24 (Normal)	180 (74.7%)	184 (76.3%)
25-29 (Overweight)	58 (24.1%)	53 (22%)
>30 (Obese)	03 (1.2%)	04 (1.7%)
Parity		
Multigravida	119 (49.4%)	110 (45.6%)
Primigravida	122 (50.6%)	131 (54.4%)
Post-Operative Wound Infection		
Present	4 (1.7%)	6 (2.5%)
Absent	237 (98.3%)	235 (97.5%)

Table 2 represented the risk factors associated with postoperative wound infections. All the variables including age (OR=0.751, 95%CI=0.209-2.695, p=0.659), parity (OR=2.144, 95%CI=0.548-8.390, p=0.262), gestational age (OR=1.462, 95%CI=0.407-5.249, p= 0.558) were found insignificant with the risk of wound infection (Table. 2) while BMI found significantly associated (p=0.0001) with the wound infection. Sub-group posthoc analysis has shown that patients with Higher BMI values have a high risk for surgical site infection after caesarian section (p=0.0001).

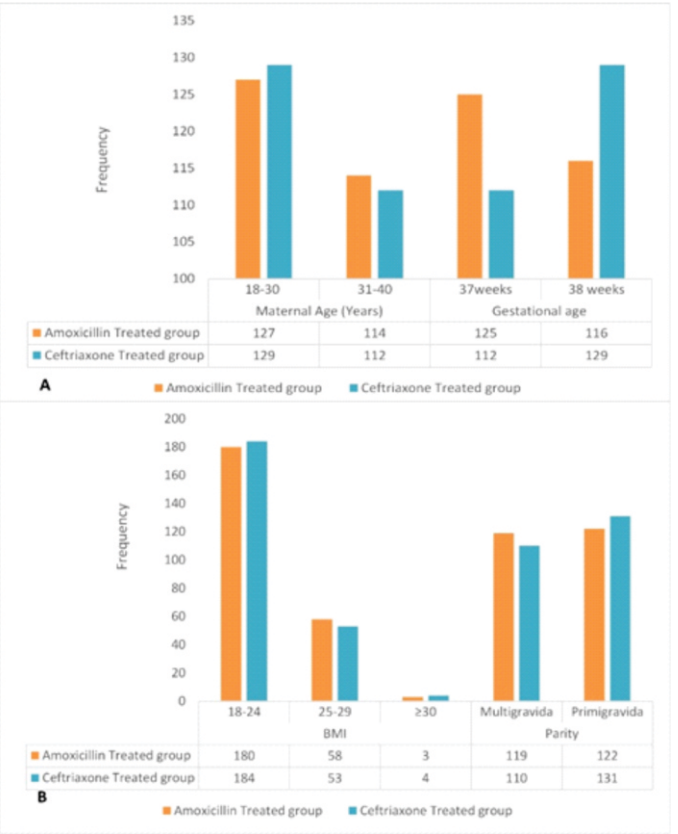

Fig-1. *Bar charts represented the frequencies of age, gestational age (A) and BMI and Parity (B)*

Table 2: *Correlation of outcomes with treatment (Amoxicillin vs Ceftriaxone), [OR: odds ratio; CI: confidence interval; p-value is considered as statistically significant when ≤0.05 (in bold)].*

Vari-able	Category	Wound infection present (Amoxi-cillin)	Wound infection absent (Amoxi-cillin)	OR (95% CI)	p-value	Wound infection present (Ceftria-xone)	Wound infection absent (Ceftriaxone)	OR (95% CI)	p-value	(OR (95%CI) Overall	p-value Overall
Age (years)	18-30	3 (2.4%)	124 (97.6%)	0.366 (0.38-3.567)	0.368	3 (2.3%)	126 (97.7%)	1.156 (0.229-5.845)	0.861	0.751 (0.209-2.695)	0.659
	31-40	1 (0.9%)	113 (99.1%)			3 (2.7%)	109 (97.3%)				
Parity	Multigravida	1 (0.8%)	118 (99.2%)	2.975 (0.305-29.01)	0.325	2 (1.8%)	108 (98.2%)	1.701 (0.306-9.466)	0.540	2.144 (0.548-8.390)	0.262
	Primigravida	3 (2.5%)	119 (97.5%)			4 (3.1%)	127 (96.9%)				
BMI (kg/m^2)	18-24	0	180 (100%)	N/A	**0.0001**	0	184 (100%)	N/A	**0.0001**	N/A	**0.0001**
	25-29	1 (1.7%)	57 (98.3%)			2 (3.8%)	51 (96.2%)				
	>30	3 (100%)	0			4 (100%)	0				
Gesta-tional Age (Weeks)	36-37	1 (0.8%)	124 (99.2%)	3.292 (0.338-32.10)	0.278	3 (2.7%)	109 (97.3%)	0.865 (0.171-4.374)	0.861	1.462 (0.407-5.249)	0.558
	37-38	3 (2.6%)	113 (97.4%)			3 (2.3%)	126 (97.7%)				

Discussion

Caesarean delivery (CD) is linked to a greater postoperative infection rate compared to vaginal birth and other surgical procedures. As CD prevalence rises globally, such post-CD infections are anticipated to constitute a serious health and financial burden. Results from past research have clear evidence that CD antibiotic prophylaxis works to reduce maternal infection morbidity along with cost-effective treatment. These advantages extend to both scheduled and unscheduled (emergency or laboring) CD. A single selective antibiotic may have equal effectiveness compared to multiple doses of a combination of antibiotics.[9] The best medication for surgical prophylaxis should be long-acting, affordable, and have few side effects.[9,17] The most used antimicrobial for prophylaxis in obstetricians is usually cephalosporin. Ceftriaxone and Amoxicillin and other similar class of antibiotics has already been proven to be effective antibiotics for the prevention of postoperative infection morbidities after caesarean section by numerous earlier research.[18,19]

In this study, we compared the effectiveness of preoperative administration of two important preventive antibiotics at cord clamping, with the primary outcome as the presence of wound infection after CS birth. We had to use an intravenous dose of 1gm for four days followed by oral administration of 250mg 6-hourly for both antibiotics in their respective treated group cases. Our study provided data on the frequency of surgical site infections in a hospital where prophylactic antibiotic administration before skin incision and consistent weekly operating room cleanliness was observed. The overall rate of 4 (1.7%) and 6 (2.5%) for amoxicillin and ceftriaxone respectively, is low when compared to the prevalence of SSI in developing nations, but this is also plausible because certain studies conducted in hospitals with good medical equipment have revealed even lower incidence. Both prophylaxes have shown insignificant differences while observing protective effects against wound infection. Interestingly, the morbidity rate in our trial was found lower as compared to the study of Igwemadu et al. and Mohn et al. where they reported 7.4% and 5.8% morbidity rates respectively.[20,21] Our findings are also strengthened by the previously reported studies in Asian ethnicities by Mudholkar et al.[22] and Ansari et al.[23] where they reported 0.3% and 2% cases respectively, of surgical wound infection.

Due to the poor socioeconomic status of the participants, the average low number of prenatal visits, and the likelihood of lengthy labor before surgery, our study population could be considered to have a high risk for infection given the recognized risk factors for postcesarean infection. Additionally, because most women only visit the hospital during labor, a significant portion of caesarean sections performed in low-resource settings can be categorized as emergency operations with a higher risk of infection than elective procedures. Taking into account all the liable factors for infections and other complications, both prophylaxes have shown significant protective effects in the local population hence the treatment can be used for the general population in the future based on further studies with a large sample size.

The only limitations of this study are the small sample size and single center. Additionally, following the Helsinki declaration (1975), amended in 2000, the current study received complete approval from the institute's ethical review board.

Conclusion:

In conclusion, the present study revealed the significance of the use of prophylactic (amoxicillin and ceftriaxone) as a preventive measure for post-operative caesarean wound infection in women. BMI was significantly associated with the risk of wound infection. However, because of the lower number of SSI that we anticipated and the tendency to have more cases in the group, we recommend the conduct of a rigorous multicenter study or a study with a large sample size confirming the absence of any difference in both groups. Further studies with other prophylactics may provide a pathway to the policymakers for constructing a strong policy regarding public health.

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Authors Contribution

AAU: Conceptualization of Project
SI: Data Collection
FJ: Literature Search
FI: Statistical Analysis
AK: Drafting, Revision
AAU, MS: Writing of Manuscript

A Comparative Study on Pre-and Post-Covid Paediatric Admissions in Pakistan

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Abstract

Objective: The COVID 19 pandemic brought with it a complex pattern of changes in society behaviour especially in access to healthcare which was seen in markedly reduced trend of paediatrics hospital admissions worldwide. The aim of this study to see if a similar trend was present in Pakistan by comparing the number and characteristics of paediatrics inpatients in a tertiary care hospital.

Method: Retrospective cross-sectional study performed on patients aged 1-12 years admitted in paediatric ward of Punjab Rangers Teaching Hospital, Lahore during the year before Covid-19 pandemic, i.e., March 2019- February, 2020 and the year after the pandemic in Pakistan, March, 2020 - February, 2021. Data collected from hospital medical records included the number of paediatric admissions, admissions of infectious vs. non-infectious illnesses with special focus on Acute Respiratory Illness (ARI) and Acute Gastroenteritis (AGE) and whether patients were pre-schoolers or school-going children. The data was analysed using SPSSv.21.

Results: A decrease of 50% in Paediatric admissions was seen in post-Covid period which was significant (P-Value 0.001 (95% CI 17.6 – 54.3)). The fall in admissions of school-going children was more significant (P-Value <0.001) compared to preschool age admissions (P-value 0.026). Infectious disease was 70% of the admissions but fell by 60% after the pandemic started (P-value <0.001). There was a significant reduction in admissions with both ARI (P-value 0.049) and AGE (P-value 0031) in pre-school children.

Conclusion: Our study demonstrates that there was a significant decrease in paediatric hospital admissions during the pandemic. This is suggestive that patients may have avoided or refused necessary healthcare due to fear of contagion.

Keywords: Post-Covid, Paediatric Admissions, Pakistan

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Introduction

World Health Organization declared a new pandemic of Severe Acute Respiratory Syndrome Coronavirus 2 disease on 11th March, 2020.[1] The 1st case of Covid-19 infection in Pakistan was reported on 26th February, 2020 and the wave peaked in June, 2020.[2] An extended lockdown from late March, 2020 and multiple measures taken at government level helped bring the numbers down by July, 2020. However, the gradual easing of restrictions and resumption of social and business activities led to the second wave of Covid epidemic, declared on 28th of October, 2020.[3] To date there have been 1.5 million confirmed cases of Covid in Pakistan with around 30,500 confirmed deaths.[4]

The pandemic of SARS-COV-2 has remained a mild, self-limiting respiratory illness in children, as shown in a systematic review of 1065 children infected with Covid, with only 2% requiring intensive care[5,6]. However, children and their families have been affected in other ways due to the imposition of lockdown and public health measures, such as social distancing, to contain the pandemic. By the 1st of April, 2020, 194 countries had enforced school closure in an effort to control the

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pandemic by limiting child-to-child transmission of viral illnesses.[7] During the lockdown period, movement outside of homes was strongly discouraged, only allowed in case of medical emergencies. This social isolation was aggravated by the pervasive fear of contagion and increasingly suspicious attitudes towards larger communities.[8]

One of the major resulting effects noted from this was the decreasing trend in hospital admissions of paediatric population. Access to healthcare along with education and social services are basic facilities in place to ensure and maintain the well-being of a growing child, which is why the decline in hospital admissions should be investigated further.[9] Besides that, it is more worrying that many children suffering from chronic illnesses may have been deprived of healthcare during the lockdown and may have compounded the morbidity of their condition.

Imposing lockdown for any time period had serious implications and did not only have a limiting effect on COVID-19 spread but also on all other transmissible infectious diseases.[10] This effect is more pronounced in the pediatrics field, since 28% of diagnoses in pediatric emergency departments (EDs) are due to infectious disease.[11] As it was expected, a fall in the total pediatric admissions and visits to the emergency department (ED) has followed lockdowns worldwide.[12,13] However, it is not clear whether this decrease is only due to a decrease in transmissible infections or by changes in behavior around healthcare utilization, as well. As an example, there have been numerous reported examples of avoidance of care due to fear of a hospital environment, which is potentially disastrous.[14,15]

This study focuses mainly on the impact of the pandemic on access to health services for children and their families, in Pakistan. The objective was to compare the number of admissions Pre-Covid and Post-Covid periods in a tertiary care hospital. We further looked into how the admission of cases of major infectious diseases of a developing country, such as Acute Respiratory Infections (ARI) and Acute Gastroenteritis (AGE), were affected by the Covid-19 pandemic in pre-school and school-going children.

Material and Methods

We carried out a retrospective cross-sectional analysis in the Paediatrics Department at a tertiary care set-up, Punjab Rangers Teaching Hospital (PRTH), Lahore, Pakistan. All cases of paediatric inpatients (1 month - 12 years) admitted in the one-year period before Covid pandemic (March, 2019-February, 2020) and one year post-Covid (March, 2020-February, 2021) were included in this study.

We obtained patient demographics from medical records and the number of admissions in total. The diagnosis of ARI and AGE were tabulated specifically. Further variables analysed were the number of paediatric admissions with infectious vs. non-infectious diseases and the pattern of admissions in pre-school (<5 yrs) and school-going children (5-12 yrs.) in pre-Covid and post-Covid period.

The data was entered on Microsoft application v.16 and analysed using SPSS statistics software application v.21.

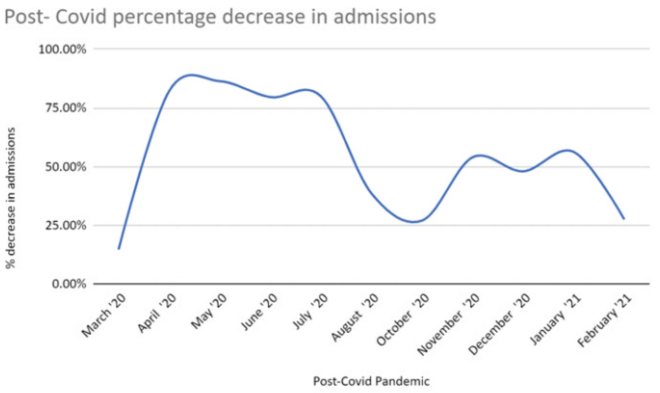
Results

There were a total of 883 admissions in PRTH, Paediatrics department between March 2019 and February, 2020 compared to 452 admissions after the advent of Covid-19 Pandemic, the following year between March, 2020 and February, 2021. This is a fall in paediatric admissions by almost 50%. On application of paired t-test between admissions of pre-covid and post-covid there is significant difference between means and standard deviations of total cases per month for each year at a P-Value of 0.001 (95% Confidence Interval 17.6 – 54.3) (Tab 1). Comparing the months of April-May 2019 and April-May 2020, there was more than 80% decrease in admissions following the lockdown imposed on 24th March, 2020. At the time of the second wave of Covid in late October, 2020 the admissions in November-December, 2020, decreased by around 50% compared to the same months in 2019. (Fig. 1)

Fig. 1- *The Percentage of Decrease in Paediatric Admissions in Post-Covid Period.*

Table 2: *Comparison of Decrease in Paediatric Inpatients between 1st and 2nd wave of Pandemic*

Time Period	Mean % decrease in admissions from Pre-Covid time	P-value
1st wave April '20 – July '20	82.2%	**0.013**
2nd wave November ' 20 - January '21	52.6%	



The ratio of pre-school to school-going children was 3:2 and remained mostly unchanged in the post-Covid time period. The number of Preschool children admitted in paediatrics ward declined significantly from at a mean difference of 15.8 with standard deviation of 21.4. (Tab. 2) This was significant at a P-Value of 0.026 (95% CI 2.2-29.4). In case of school-going children, the difference in admission between pre-Covid and post-Covid years was more significant at P-Value of <0.001 (95% CI 11.9-26.5). Both pre-school children and school-going children at a decreased admission percentage of 57.9% and 65.3% respectively.

Infectious diseases made up almost 70% of the bulk of paediatric admissions in the Pre-Covid period with ARI compromising 19.9% and AGE 25.5% of the illnesses. The total no. of inpatients with infectious illnesses reduced significantly at a mean of 31 (P-value <0.001, 95% CI 17.26-44.9). (Tab. 1 Fig 2) The admissions with non-infectious illnesses reduced but it was insignificant (P-value 0.091, 95% CI 1-11.9). ARI and AGE both made up 25% each of hospital admissions post-Covid with infectious illnesses.

Preschool children were largely affected by infectious diseases at 62% compared to school-going children. The no. of patients with infectious diseases fell by 60.7% post-Covid, of which ARI fell by 51.2% and AGE by 60.6%. It was observed that even though the reduction in total admissions with ARI fell by more than 50% which was insignificant (P-value 0.057, 95% CI -.18-10.5), the fall in pre-school age ARI admissions by 56% was significant (P-value 0.049, 95% CI 0.03-9.96). Reduction in the number of school-going children with ARI was not significant (P-value 0.72, 95% CI -1.26-1.76).

The decrease in Total AGE admissions by 60.06% and of Pre-school admissions with AGE by 58.9%, in pre-Covid period, were both significant at P-value 0.026 (95% CI 1.08-13.74) and P-value 0.031 (95% CI 0.76-13.41), respectively.

Table 1: *Paired Differences T-test on Total Admissions, Infectious vs. Non-Infectious, ARI and AGE Admissions*

Subgroups comparison Pre- vs. Post-COVID	Paired Differences		P-value
	Mean	95%CI	
Total Admissions	35.91	17.56-54.2	0.001*
• Preschool Age	15.83	2.23-29.44	0.026*
• School-Going Age	19.25	11.98-26.52	<0.001*
Infectious Illnesses	31.08	17.26-44.9	<0.001*
• Preschool Age	18.33	7.06-29.59	0.004*
• School-Going Age	12.75	8.61-16.88	<0.001*
Non-Infectious Illnesses	5.16	1-11.29	0.091
Total ARI[1] Admissions	5.16	-.18-10.5	0.057
• Preschool Age	5.0	0.03-9.96	0.049*
• School-Going Age	0.25	-1.26-1.76	0.723
Total AGE[2] Admissions	7.41	1.08-13.74	0.026*
• Preschool Age	7.08	0.76-13.41	0.031*
• School-Going Age	0.33	-0.54-1.20	1.417

**2-tailed t-test observed difference was statistically significant.*
[1] Acute Respiratory Illnesses.
[2] Acute Gastroenteritis

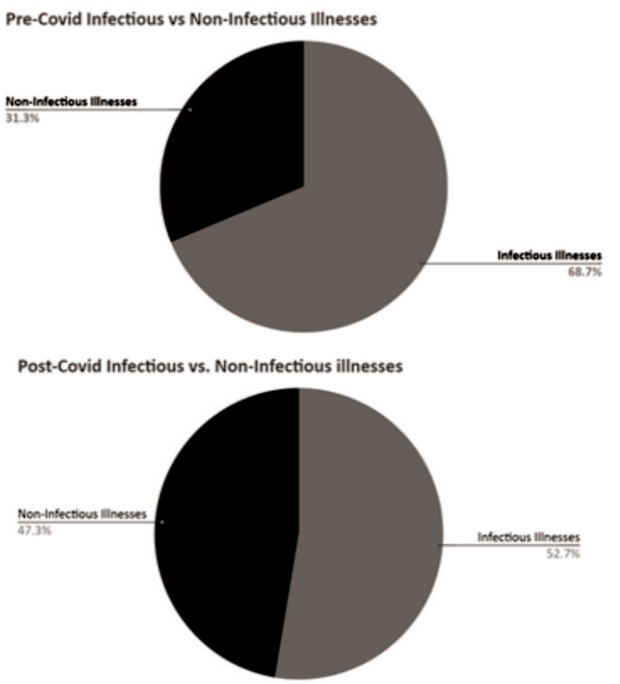


Fig. 2- *Comparison of Hospital Admissions with Infectious vs Non-Infectious Illnesses in Pre-Covid and Post-Covid Time Period*

Discussion

This retrospective observational study has shown that there has been a significant reduction in paediatric hospital admissions by almost 50% (P-Value 0.001, 95% CI 17.6 – 54.3) since Covid pandemic compared to pre-Covid time period, in Pakistan.

A similar decline in paediatric admissions were reported in Italy, United Kingdom and United States. Isba et al. reported a fall in UK Paediatric Emergency department attendances in February and March 2020 by 5.6% and 30.4% respectively compared to the same months in 2019, following the UK lockdown implementation from 23rd March, 2020.[12] Similarly, in Pakistan, when we compare the months of April-May 2019 and April-May 2020, there was more than 80% decrease in admissions following the lockdown imposed on 24th March, 2020. In the US, Nourazari et al. also reported 32% reduction in admissions between week 11 and 36 in 2020.[16] In Northern Italy, Rabbone et al. observed a 73.2% reduction in total paediatric admissions in the year 2020 compared with the same period in 2019.[17]

In our study, there was a sharp fall in number of paediatric admissions with infectious illnesses (P-value <0.001) with the start of the pandemic. This was especially significant in pre-school age children, in whom there was a decrease in admissions with both ARI (P-value 0.057, 95% CI -.18-10.5) and AGE (P-value 0.026, 95% CI 1.08-13.74). This was also the case in Northern Italy, during Covid-19, where there was a significant (p< 0.001) drop in infectious (-51%), respiratory (-25.5%), and nervous systems diseases (-50%).[17, 18] The fall in ARI admissions in children under 5 years of age, which included paediatric asthma cases, could be attributed to the improvement of the Air Quality Index (AQI) during lockdown in combination with the reduced transmission of viral respiratory infections. There is a significant association between increased AQI and severity of lower respiratory tract infection in children under 5 years of age.[19]

The drop in number of admissions to our paediatric department was not as marked around the 2nd wave of the Covid-19 pandemic as the first wave. Since the start of extended lockdown in April 2020 the number of admissions decreased by 80% compared to the year before and remained so until July 2020. Thereafter a rise in paediatric inpatients was seen with a higher number of admissions in September 2020 compared to September 2019. From November 2020, with the advent of second lockdown the number of admissions decreased again but by only 45-50% from the same months in 2019. The percentage of decrease in admissions from the government-imposed lockdown at the time of the 1st wave of pandemic was higher by roughly 30% compared to the decrease in hospital admissions around the second wave, which was significant (P-value 0.013, 95% CI -38.4—12.9) This could be attributed to the less strict adherence to SOPs at a public level. This resistance to social distancing and SOP in Pakistan, was observed by Elahi et. al and it was found that the major determinant of this behaviour was low literacy level.[20] Similar behaviours were noted across the globe, such as in Spain, Gualda et.al observed that the reason behind the lower compliance to SOPs were sociodemographic factors, personal hygiene patterns, and lack of trust in political institutions. Less compliance was also associated with beliefs in some specific conspiracy theories with regard to COVID-19.[21] These factors may also be relevant in the Pakistani population and deserve more insight to combat any future pandemics.

Exploring the reasons behind the sharp decline in post-Covid paediatric admissions is likely to be multifactorial. Imposition of lockdown led to isolation from large gatherings, following SOPs, including social distancing, wearing masks and handwashing. The fear of contagion in general public most likely led to avoidant behaviour in seeking healthcare services. From a study by Dan et. al, in a busy Irish hospital, due to a combination of factors, there was a reduction in presentations widely accepted as mediated by viral exposure (wheeze, bronchiolitis and febrile convulsions); reduction in school-related stress (headaches and abdominal pain); and parents deciding to stay at home due to fear of attending during the pandemic, with non-emergent conditions (neonatal feeding issues, vasovagal episodes and non-anaphylactic allergic reactions). Injuries, scalds, ingestions and foreign bodies became less frequent, likely because of fewer outdoor activities and more supervision by parents.[22]

The point of concern here is that reduced access to healthcare facilities due to priority given to Covid patients combined with fear of carers/guardians to exposure to Covid affected at a hospital, may have led to delay in seeking treatment for seriously unwell children, especially those with chronic ailments. In a nationwide NHS England study by Etoori et.al, one in six clinically vulnerable children accounted for almost half of the reduction in hospital care during the pandemic.[23] The inability to carry out routine healthcare for complex illnesses and

disruption of vaccination schedules has increased the risk of emerging diseases.[24] An improvement in Air Quality Index, during lockdown, also brought about a reduction in acute exacerbation of asthma and other respiratory ailments in children.[19]

Conclusion

In conclusion, the significant reduction in total paediatric admissions, especially of infectious ailments in children under 5 years, during the Covid-19 pandemic, has driven major changes in paediatric practice and leaves many lessons for us to learn for future pandemics. It is justifiable to introduce telemedicine and virtual access to healthcare, especially to children with chronic ailments. There is also requirement of ensuring that mental and emotional well-being of families and children is cared for.[25] To combat the avoidant behaviour of following SOPs we need to educate and build trust with the general population, through national programs. Further research is required to assess the consequential damage that has taken place in Pakistan during the pandemic.

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ASQ: Writing of Manuscript

MA: Data Collection

SN: Literature Search

MA: Statistical Analysis

ZA: Drafting, Revision

MAK: Conceptualization of project

Comparative Efficacy Of Manual Vacuum Aspiration And Medical Termination In First Trimester Miscarriage

Natasha Bushra,[1] Javeria Zunair,[2] Lamia yousaf,[3] Ameelia Sadaqat[4]

Abstract

Objective: To compare the efficacy of medical termination versus manual vacuum aspiration in first-trimester miscarriage.

Method: This was a quasi-experimental study done at Department of Obstetrics and Gynaecology Services, Institute of Medical Sciences Lahore from January to September 2018. Women who chose medical termination were offered 600 micrograms of misoprostol given sublingually and dose repeated after 3 hours. Patients were chosen manual vacuum aspiration and were explained the method, informed consent was taken, and MVA was performed after cervical ripening. A designed proforma was filled in terms of pain score, amount of blood loss, and general symptoms like fever and diarrhoea.

Results: Of all women who were enrolled in the study were 408. Out of the medical termination was chosen by 228(56%) and manual vacuum aspiration was selected by 180(44%). For those patients who chose medical termination, the majority of them had fear of intervention i.e., almost 77% followed by a fear of infection after surgical intervention (62%). Patient with medical termination experienced more pain and increase blood loss as compared to MVA($p<0.05$).

Conclusion: MVA is a safe and effective method for early pregnancy termination as compared to medical termination

Keywords: Manual vacuum aspiration, medical termination, efficacy

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Introduction

Miscarriage results in 10–20% of clinically recognised pregnancies. A large number of women present in tertiary care hospitals for treatment of the miscarriage or complications related to abortions. Unsafe abortions are a key contributor to maternal morbidity which is one of the determinants of Millennium Development Goal (MDG) targets.[1] It causes 13% of maternal mortality in developing countries and accounts for 99% of maternal death worldwide. In Pakistan, complications due to miscarriage cause maternal mortality upto 10-12%. Studies show that large number of women seeking for abortion are not educated and are not practicing any contraception. They have limited resources to report any tertiary care hospital and that lead to unsafe abortions. The most common reason for abortion in Pakistan is limitations to practice of contraception due to social and cultural backgrounds.[2]

The health care professionals in Pakistan are striving hard to provide safe abortion services to the community and to avoid the abortion related complications that will further facilitate in achieving the sustainable development goal 3 which calls for good health and well-being.[3]

Induced abortion by untrained quacks is one of the leading causes of maternal mortality and morbidity.[4] Diffe-

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rent methods of termination of pregnancy are being used and in the recent years MVA has gained popularity not only being safe and simple and more cost effective, but also leads to less complications and shorter hospital stay as compared to others. Medical termination of pregnancy by prostaglandins is an alternative method and most widely used drug is prostaglandins A study conducted in northwest Ethiopia concluded that women undergoing medical abortion are more satisfied than surgical abortion and it can be offered as an alternative method especially in low resource settings.[5]

Another study conducted in USA in 2012 compared different options for early miscarriage and concluded that expectant management leads to increase risk of bleeding that may need blood transfusion and emergency need for surgical evacuation. This study included 1521 participants. The group offered expectant management had retained products of conception seen on ultrasound after 3 weeks (RR 4.0; 95% CI 3.14 to 5.38) or by six to eight weeks (RR 3.1 95% CI 1.15 to 6.29). The mean percentage of additional surgical management in the expectant group was 28%, while only 4% in the surgical-treatment group. The expectant group had bleeding risk more than surgical group (MD 1.59; 95% CI 0.74 to 2.45. There was increased need of blood transfusion in expectant group (RR 6.45; 95% CI 1.21 to 34.42) with the mean percentage of 1.4% as compared with none for surgical management. Risk of infection was similar for the two groups (RR 0.63; 95% CI 0.36 to 1.12). [6]

A trial comparing medical and surgical options was conducted in UK that recruited 349 women concluded that medical termination of pregnancy was less costly but also less effective than surgical evacuation. Although medical treatment was more acceptable for majority of women.[7] Clinical governance is framework responsible to maintain standards in health care providers and beneficence and consent is one of its pillars. Involving patient choices and preference in making the decision about treatment options is the essential component of health care services.[8]

To address the huge population demand and to facilitate the large masses at peripheral areas still medical abortion can be considered a good choice to provide safe abortion service at home however its accept-ability in women is largely unknown. Our study aims to assess the efficacy and acceptability of medical treatment and Manual vacuum aspiration in early pregnancy termination.

Material and Methods

It was a quasi-experimental study conducted in the Department of Obstetrics and Gynaecology, Services, Institute of Medical Sciences Lahore from January to September 2018. The calculated sample size was 380 with confidence interval of 95% with 5% margin of error. The proposal was submitted in hospital ethical board. After approval from Ethical Committee, all women who fulfilled the desired criteria were included in the study. Patients with 1st trimester miscarriage confirmed by pelvic ultra-sound were explained the aim of study and the informed consent was taken. Patients were explained about options of medical termination with misoprostol and manual vacuum aspiration telling in details risks and benefits associated with both options. Women after detailed counselling chose the desired option and reason of choice with all details were noted on the proforma. Women who made choice of medical termination were offered 600 micrograms of misoprostol given sublingually and dose repeated after 3 hours according to FIGO criteria. Patients were discharged explaining to report in case of red flag signs like pain and bleeding. Women who made choice for manual vacuum aspiration were explained the method, informed consent was taken and after following WHO surgical safety checklist, MVA was performed under paracervical block. Cervical ripening with 400 microgram misoprostol was given either sublingually or vaginally. This dose is used for cervical ripening only to prevent trauma to the cervix. It will not affect the result of medical vs MVA treatment. MVA was performed by applying local anaesthesia 10-20 ml of 1% lignocaine intracervical at 2-, 4-, 8- and 10-O'clock. Products of were sent for histopathology. All patients were called for follow up after 1 week. A designed proforma was filled in terms of pain score, amount of blood loss, general symptoms like fever and diarrhea. Data was analysed though SPSS version 20. Quantitative variables like patients age will be presented by mean$\pm$SD. Qualitative variables will be presented by calculating the frequency and percentage. Post stratification chi square test will be applied keeping a p-value <0.05 as significant.

Results

All women who were enrolled in study were 380. Out of them medical termination was chosen by 228(60%)

and manual vacuum aspiration was selected by 152 (40%). Those patients who chose medical termination, the majority of them had fear of intervention i.e., almost 82%. 68% patients were afraid of hospital setting so preferred home treatment by medication. Few women chose medical treatment due to fear of infection after surgical intervention (45%). Those who chose MVA were concerned for Minimal pain in 84% women. There was fear of excessive blood loss by medical treatment that made to decide MVA in 57%. The minimal time interval taken for expulsion was main reason those who chose MVA (54%). All patients who underwent MVA had complete expulsion confirmed by post procedure ultrasound although 51(22%) of the patients who were given medical termination need to undergo dilatation and curettage($p<0.05$). The time span in average for patients who had medical termination was upto 24 hours-48 hours. Patient with medical termination experienced more pain and increase blood loss as compared to MVA ($p<0.05$). No case with pelvic infection was reported in both groups. The comparison of outcomes in patients underwent MVA and medical termination is shown in **Table 3.**

Table 1: *shows patient's characteristics*

Variables		Mean±SD Frequency(%)
Age		27±4.6
Parity	PG	147(36)
	G2 – G4	158(38)
	>G5	103(26)
Address	Urban	100(25)
	Urban Slum	234(57)
	Rural	74(18)
Education	Illiterate/ Elementary	147(36)
	Secondary	208(51)
	Higher Secondary	53(13)
Occupation	Working	71(17)
	House wife	337(83)
Contraception	Yes	100(25)

Table 2: *Reason for Choosing Medical Termination of Pregnancy*

	No%
Fear of Intervention	176(77)
Privacy at Home	143(63)
No Infection	142(62)
Shows Reason to Choose MVA	
Minimum Pain	128(71)
Fear of Excessive Blood Loss	72(40)
Short Time Procedure	91(51)

Table3: *Comparisn of Mva &medical Termination of Pregnency*

		MVA	Medical TOP	Chi-Sq	P-Value
Pain	Mild	141	37	161.32	0.001
	Moderate	39	164		
	Severe	0	27		
Haemorrh	<100ML	164	31	242.22	0.001
Age	>100ML	16	197		
Time	6 Hour	180	24	322.1	0.001
Interval	12 Hour	0	204		
Repeat Evacuation		0	64	59.927	0.001
Infection		0	0	Non significant	

Discussion

Miscarriage is a very stressful condition. Patients who are already traumatized must be handled carefully, the treatment offered should be safe effective and humane with no effect on future fertility perspective. Traditionally surgical treatment is considered best for the management of first-trimester miscarriage, but now MVA and medical treatment are considered as an alternative. The aim of our study was to compare the efficacy of MVA and the medical management of first-trimester miscarriage. In our study, 72% of patients opted for MVA due to the short procedure, minimal pain, fear of blood loss and less time is taken for expulsion. Almost similar findings were noted in another study.[9]

In our study complete evacuation was seen in all patients of the MVA group. while in the misoprostol group, 22% patients required evacuation by MVA, in another study similar findings were noted that in the MVA group, a no-repeat evacuation was required.[10] In our study pain and blood loss were significantly less in the MVA group as compared to the misoprostol group($p<0.05$). MVA is highly safe provided the health professionals are trained and equipped with proper MVA KIT. The safety of MVA can be attributed to the soft and flexible structure of pump and kitSide effects like diarrhea, fever, and vomiting were higher in the group that used misoprostol as compared to the MVA group. The results are comparable another study.[11]The results of our study revealed that MVA is better than medical management of first-trimester miscarriages. Similar findings were noted in many other studies like Tahir et al.[12] This is contrary to a study that found that both

MVA and misoprostol have the same efficacy.[13]

MVA is easy and cost effect and can be performed in outpatient clinics and theaters with less man power and equipment resources as it does not require sedation and anesthesia machines.. In poor countries like ours where anaesthesia staff and facilities are less and operation theatres are heavily occupied, MVA can be a safe option for the management of first-trimester miscarriages.[14]

In our opinion Careful patient selection and effective counselling can give better results. Hospitals should arrange for MVA kits. Proper training of staff should be done on regular basis We must conduct and get patients' feedback to improve this outdoor procedure and reduce hospital inpatient burden. We recommend conducting qualitative studies to know the perspective and insight depth of patients feeling while using MVA or medical treatment for the management of first trimester miscarriages.

Conclusion

Manual vacuum aspiration is a safe and effective method for early pregnancy termination as com-pared to medical termination with misoprostol.

Conflict of Interest: *None*

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Authors Contribution

NB, AS: Conceptualization of Project

JZ: Data Collection

NB, JZ: Literature Search

JZ, AS: Statistical Analysis

NB, LY: Drafting, Revision

NB, LY, AS: Writing of Manuscript

Polycythemia Vera with Metastatic Adenocarcinoma in Bone Marrow of A 68 Year Old Male

Umera Saleem,[1] Hamza Tariq,[2] Farva Komal,[3] Hajrah Syndeed,[4] Muhammad Samiullah[5]

Abstract

The co-occurrence of polycythemia vera (PV) and metastatic adenocarcinoma in bone marrow is rare. The present case study describes a case of PV in association with metastatic carcinoma in the bone marrow. Magnetic resonance imaging (MRI) pelvis (for hip joints) revealed suspicious bone marrow changes in the lumbosacral spine. The bone marrow biopsy indicated hyperplastic trilineage hematopoiesis along with non-hemopoietic cells. The findings of immunohistochemistry on the trephine biopsy sample indicated the gastrointestinal origin of metastatic non-hematopoietic cells. The present study may help in the future management of patients with polycythemia vera and metastatic adenocarcinoma.

Keywords: myeloproliferative neoplasms (MPN), polycythemia vera (PV), solid cancer, metastatic adenocarcinoma

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Introduction

Polycythemia vera (PV), a myeloproliferative neoplasm (MPN), is associated with increased RBC production, panmyelosis and JAK2V617F or JAK2 exon 12 mutation.[1] It has a prevalence of 22 cases per 100,000 population.[2] Recent studies have shown that MPN patients have almost double the chance of developing solid tumours such as lung, GIT, kidney, prostate, ovary and bladder as compared to the general population.[3]

We present a case study of a 68-year-old man suffering simultaneously from PV and metastatic adenocarcinoma. We believe it may be the first case report of PV, diagnosed using World Health Organization (WHO) criteria,[1] that has been linked to metastatic adenocarcinoma. Future diagnosis and treatment of patients with metastatic adenocarcinoma and PV may benefit from the results of the current report.

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Case study

A 68-year-old man presented in medicine outdoor with a history of backache and left leg pain for 1.5 months. There was no fever, shortness of breath, chest pain, dyspepsia, melena, cough, abdominal or urinary symptoms. He had a transient ischemic attack 20 years ago but didn't take any treatment. The patient gave the history of one episode of per rectal bleeding a few years back, but it was not investigated and resolved without any treatment. The patient was a non-smoker and had no chronic respiratory illness. General physical examination revealed facial flushing and palmar erythema, and a single left inguinal lymph node 2×2 cm. The neck was supple, and the thyroid was non-palpable. On examination, the prostate was mildly enlarged with no palpable nodularity. Systemic examination was unremarkable. His CBC showed RBC Count= 8.26×1012/L, Hb=21.2 g/dL, HCT=67.1 %, MCV=81.2 fL, MCH=25.7 pg, MCHC=31.6 g/dL, TLC=10.1×103/µL, Neutrophils = 82 %, Lymphocytes=12 %, Monocytes=04 %, Eosinophils = 02 %, Retics= 2.8%, Platelets=339×103/ µL.

Peripheral smear showed polycythemia and target cells, neutrophilic predominance and platelet anisocytosis with few giant platelets (Figure#1).

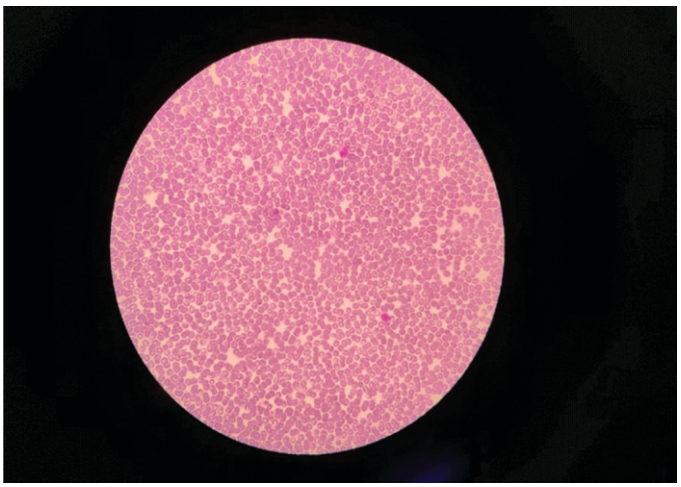

Figure 1: *Peripheral Smear Showing Polycythemia and Target Cells*

Coagulation profile, random blood glucose and renal parameters were normal. Serum potassium was 6.4 mmol/L, and serum sodium was 131mmol/L. Liver function tests revealed AST=92U/L, but total bilirubin, ALT, and alkaline phosphatase were normal. Viral markers were negative. USG abdomen showed bilateral renal parenchymal echogenicity (Grade I) and moderately enlarged prostate. X-ray lumber spine and pelvis were normal. Serum PSA was 2.8 ng/ml. Serum CRP was 1.3mg/dL and ESR was 4mm/1st hr.

MRI pelvis revealed no abnormal findings in pelvic viscera, but degenerative changes in hip and sacroiliac joints along with suspicious signals in the lumbosacral spine, were noted. Mild inflammatory changes were noted in the soft tissue around the left iliac bone. Bone marrow biopsy revealed hypercellular fragments and cell trails with panmyelosis and 2% blasts. Trephine biopsy revealed panmyelosis with pleomorphic megakaryocytes. (Figure#2)

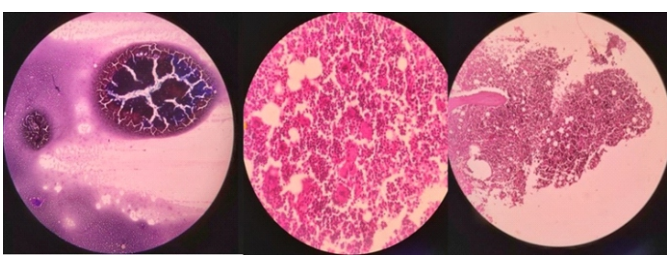

Figure 2: *Hypercellular Aspirate and Trephine Showing Panmyelosis*

Touch imprints and trephine revealed focal clusters of non-hemopoietic cells, which were large in size with hyperchromatic nuclei and prominent nucleoli (Figure # 3)

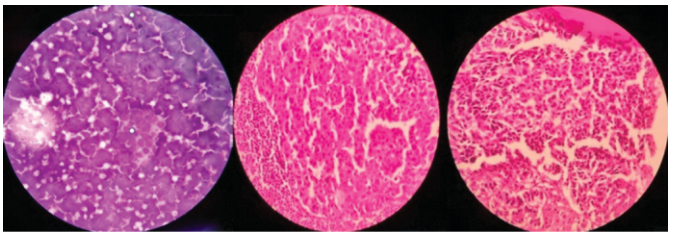

Figure 3: *Metastatic Cells in Touch Imprints and Trephine Biopsy*

The detection of JAK2 V617F mutation by PCR was positive. The serum erythropoietin level was 2.15 IU/L (reference range: 4.3 to 29 IU/L). Immunohistochemistry revealed CD45, PSA, TTF1 and Napsin-A negative in infiltrating cells. However, cytokeratin and CDX2 were positive in infiltrating cells. A diagnosis of PV with metastatic adenocarcinoma was made. Further investigations were planned, including radiological workup (CT chest and abdomen), biopsy of inguinal lymph node and upper/lower GI endoscopy to determine the site of the primary tumour. But before further workup could be done, the patient suddenly collapsed and died. We couldn't find the primary site of cancer as the attendants of the patient refused autopsy.

Discussion

Polycythemia vera is a clonal disorder that is typically associated with JAK2 mutations (V617F or exon 12).[1] Primary polycythemia is caused by bone marrow disorders, and secondary polycythemia develops as a result of other conditions, such as solid malignan-cies.[4] Malignancies of the prostate, breast, lung and gastrointestinal system commonly metastasize to the bone marrow but can be missed due to their cryptic presentation. Early detection of bone marrow metastasis is crucial as most cases exhibit bone marrow metastasis before the detection of primary tumour.[5] Patients with MPNs are more prone to having second primary solid tumours such as lung, thyroid, GIT, kidney and melanoma.[3] The identification is important as co-occurrence might affect long-term survival. The underlying mechanism might be genomic instability, cytotoxic medications, chronic inflammation and immune dysregulation.[6] Literature search shows that, especially for colorectal malignancies, the JAK-STAT pathway is proposed to play a critical role in the systemic inflammatory response.[7] Metastatic carcinoma from an unidentified primary

site presents a clinical problem. The metastatic cells of our patient were positive for cytokeratin, which points to epithelial origin. PSA, Napsin-A and TTF1 were negative, ruling out possibilities of prostate, lung and thyroid tumours. CDX2 was positive in our patient's metastatic cells. Therefore, we infer that our patient most likely had bone marrow infiltration by colorectal malignancy in addition to PV. We believe that it may be the first case report showing PV along with metastatic carcinoma in the bone marrow that is of gastrointestinal origin. The literature search revealed a 73-year-old male who developed carcinoma stomach eight years after diagnosis of PV.8 Another case was reported in which a 59-year-old man having PV was found to have ascending colon cancer.[9] But none of these cases reported marrow infiltration by metastatic carcinoma in association with MPN, while our patient presented with bone marrow infiltration. Few case studies have been published showing the relationship of PV and prostatic adenocarcinoma. In these patients, localized malignancy has been reported.[10] Our patient didn't have any symptoms, signs or radiological evidence of CA prostate and his serum PSA was also normal. From our study and literature review, we conclude that patients with PV have a high incidence of solid tumours, especially adenocarcinoma. But we are currently unsure if this relationship is merely coincidental or causal. Additional studies are required in this regard, as it can jeopardize the long-term survival of patients with PV. In order to prevent missing or delayed diagnosis, the doctor should be aware of the potential link between PV and metastatic adenocarcinoma. Our case may be the first instance of metastatic cancer in the bone marrow with a confirmed PV diagnosis.

Conclusion

Several mechanisms underlie the pathogenesis of secondary malignancy in patients with PV. Future studies are needed to evaluate these pathways. Careful examination of bone marrow and other diagnostic modalities is pivotal to identify such unusual presentations so as not to miss the diagnosis.

Conflict of Interest None

Funding Source None

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The inclusion criteria of the study participants, which may be patients, healthy controls or healthy subjects, should be clearly described. Exclusion criteria need to be explained.
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Recognized the method, procedures and any equipments (manufacturer's name and address) in detail so that workers easily reproduce them and also give references to establish methods including statistical method . All drugs and chemicals should be described in generic name(s), dose(s), and route(s) of administration.

Statistics

Simple way is used to describe statistical method so that reader enable to access the original data to correct the results. Statistical software should be mentioned.

Results

- Results should be described in a logical sequence in the text, tables and illustrations.
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- Frequencies and percentages both should be mentioned.
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- Mean should be with standard deviations.

Discussion:-

Summarize main results and compared with results of other published studies.
Emphasize new findings of research.

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