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Artificial Intelligence, the Need of the Hour

Sarwat Hussain

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Introduction

Fourth Industrial revolution is currently sweeping the high-income countries (HIC) with Artificial Intelligence (AI) based automation affecting virtually every aspect of life. The term AI was first coined by McCarthy in 1956. It was not until 2000s that AI began to thrive. The evolution of AI into the current status occurred in the last decade owing to the enhanced computing power using Graphic Processing Units (GPU), development of high-powered computer languages, and the emergence of the Big Data. The latter is generated through wireless communication between 'Smart' sensors/devices and self-learning machines. The word 'smart' is applied to any device that has memory and is able to connect with data networks such as the internet and the processors. In the last few years, there has been exponential growth in AI applications. This can be judged by the projection that the AI field will add \$ 15 Trillion to global economy, by the year 2030, up from \$ 600 Million in 2016. This will occur mostly in the HIC. The adoption of AI by low- and middle-income countries (LMIC) lags far behind that of HICs. The LMICs would miss out in the economic benefits, further widening the global inequalities.

Machine Learning and Deep Learning are branches of AI that are beginning to form the basis of the automation of financial and business decisions, and are the tools of self-driving cars, industrial production, data analytics, quality improvement and healthcare processes to name a few. In healthcare, some of the AI applications have shown to enhance patient care, reduce medical errors, support clinical and administrative decision making, automate equipment maintenance and help reduce operational cost. For instance, AI led cost reductions achieved up to 25

percent drop in the length of hospital stay and up to 91 per cent reduction in admissions to step down facilities. In the United States alone, by the year 2026, AI in healthcare is estimated to realize \$150 billion in annual cost savings.

Artificial Neural Network (ANN), another branch of AI, has made Computer Vision possible. In radiology, pathology, dermatology and ophthalmology, images lend themselves to classification into malignant and benign lesions on mammography and histopathology, confirm presence of diabetic retinopathy and diagnose skin lesions. All this can be achieved by primary care doctors and nurses after some training on the related equipment. In laboratory medicine, AI is employed in precluding unnecessary tests, improving patient safety, and initiating alerts for abnormal results. In advanced laboratories of molecular/genomic testing, AI can be used to accurately identify genetic variants and match up with possible treatments.

Medical Robots, using AI technology, are assisting doctors from minimally invasive procedure to open heart surgery. Humanoid robots work for indigent patients, distribute medication and documents within the hospital premises, and help engineers in equipment maintenance.

In the many low-income countries, AI is limited to medical imaging and clinical laboratory machines. Computed Tomography, Magnetic Resonance Imaging and mammography machines usually have computer assisted image detection capability, and in laboratory equipment abnormal results alerts. These functions are embedded in the machine software as part of the purchase price.

So far adoption of AI technology in Pakistan has been mostly by default. In the social domain, the ubiquitous 'Siri' of iPhone is one example of AI's application of Natural Language Processing (NLP) and Machine Learning. Of late Pakistan's banking has made signi-

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ficant progress in implementing AI solutions. There are other pockets of AI in Pakistan. As of April 2020, there were 31 AI start-up companies in the country. Of the 174 public and private universities, accredited by Higher Education Commission, only 6 universities and 15 other colleges offer advanced education in AI. In Pakistan, digital data is scant. All paper-based record in the country requires digitization. For the AI research in to be rooted in Pakistan, all future data in the public and the private domains must be collected digitally. Tremendous benefit can be derived from building AI infrastructure, because the nation is rich in young and highly intelligent human resource. Sixty five percent of 220 million Pakistan population is under 30 years of age. Enough of these individuals must be trained to realize full economic and human services potential of AI technology.

A question commonly asked in medical circles, “will AI replace the doctors in the future”. The answer would be, doctors who are AI educated will replace in those who are not, especially those physicians seeking to work in the West. Currently the role of AI is entirely assistive and supportive. The complexity of the medical sciences will probably prevent AI from taking over physician’s functions completely.

As AI is evolving, it is important to recognize that it is not a silver bullet for the society. In fact, significant issues of transparency, regulatory control, ethics, national security, possible misuse, and built-in biases still need to be worked out.

Notwithstanding the responsibilities of the government of Pakistan and institutions of higher learning, all educated individuals, including doctors, need to develop AI consciousness though self-education. Larger the country wide grass root foot print of the AI movement, the greater the chance of producing world class scholars and researchers for the country.

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Impact of COVID-19 Pandemic on Cancer Screening in the United States

Sonikpreet Aulakh, MBBS MD¹ & Asher Chanan-Khan, MD²

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COVID-19 pandemic has exposed vulnerabilities all across the global healthcare systems including those within the United States. A systematic evaluation of these soft spots has been crucial in order to reengineer the healthcare system for enhanced competences and superior quality of care. One area that has been undoubtedly affected is the diagnosis and management of neoplastic diseases.

The healthcare system in the US witnessed an instantaneous implementation of a “social distancing” strategy, which was implemented in an effort to flatten the infectivity “curve”. This required an urgent modification in the general administration of healthcare delivery, independent of COVID-19 infection status of a patient. For the non-COVID patients, it meant a shift from in-person to a virtual administration platform." (Royce et al., 2020) Neither the healthcare providers, nor the patients, or the hospital management were adequately prepared for this sudden transition. Various healthcare services offered through these healthcare systems were required to be triaged based upon patients' assessment of needs into either emergent, urgent or routine/non-urgent. Patients seeking services that fell in the non-urgent/routine clinical visits were encouraged to stay home until the pandemic simmered down/resolved. This strategy was erroneously predicated on a rather short anticipated duration of the pandemic. As expected, cancer screening visits were deemed non-urgent and thus most healthcare facilities in and outside the US

suspended these services, inadvertently compromising the timely diagnosis of neoplastic disorders.

Over the last 50 years, we have witnessed major improvement in survival outcomes for all cancers collectively. (Siegel et al., 2020) A significant contributions to this feat is credited to the well-established cancer screening protocols allowing early detection, timely intervention and curtailing cancer related morbidity and mortality. (Duffy et al., 2020) Published data validates that cancer screening directly translates into lives saved. (Duffy & Field, 2020) While screening algorithms are not available for all types of cancers, the *Big Five* most prevalent cancers (breast, prostate, colorectal, cervical and lung) have well defined and established screening protocols which are typically administered through primary care or cancer care centers. Despite benefit of screening, challenges have persisted in achieving maximal (or desirable) compliance by patients who are eligible for specific cancers. For instance, in the US, screening mammography is achieved in 74% of eligible women covered by commercial plans, 70% by Medicare and only 59% by Medicaid. Data on uninsured women is expected to be even worse. (Peek & Han, 2004) Among the many reasons (socio-economic status, health insurance, health education etc.) (Pruitt et al., 2009) an underappreciated factor is the *psychological limitation* in cancer screening. This factor has become far more relevant in context with the COVID-19 crisis.

The psychological limitation of cancer screening pertains to a sense of wellness among healthy individuals that foster complacency towards deferring timely need of cancer screening as established and proven through rigorous clinical

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investigations. Appropriately so, the healthcare system also equates cancer screening visits as “well visits”. They are deemed non-urgent and planned visits for which the system relies upon patients' conviction to health maintenance. As often there is no perceived imminent danger to health, patients and healthcare providers' perception of these visits is that of an elective non-urgent nature. It is therefore not surprising that patients themselves, and the healthcare teams ascribed a low priority to cancer screening during the COVID-19 pandemic. This not only allowed much needed healthcare resources to be diverted to those actually fighting the COVID-19 infections, but also prevented unnecessary risk of exposure to those individuals who were not in urgent need of medical evaluation. Given this psyche, a nationwide decrease in cancer screening visits was recorded during the COVID-19 crisis. (Cancino et al., 2020) (Van Haren et al., 2020)

Another reason that directly impacted cancer screening visits, is the perceived risk of contracting COVID-19 when visiting a healthcare facility. Are all healthcare facilities truly high-risk environment for COVID-19? The drastic disengagement of preventative services (such as that for cancer) in the wake of COVID-19 crisis undoubtedly communicated this message to the masses. Can a more informed strategy been developed to minimize the impact of COVID-19 on cancer screening? For example, in high density areas of COVID-19 (such as NYC, Chicago or Los Angeles) transient complete cessation of cancer screening programs may be reasonable. Thereby extending accommodation to healthcare facilities with a high COVID burden to dispense resources towards acutely ill patients, protect staff and non-acute patients from infectivity risk. However, in cities with low COVID density, opportunities could still be leveraged cautiously to continue to offer these preventative services through employment of innovative strategies such as Telehealth. In fact, it is now increasingly recognized that ambulatory care and stand-alone diagnostic testing facilities (with appropriate PPE) pose comparably far less risk of COVID-19 infectivity vs.

acute care hospital settings.

In reality, as the COVID-19 threat rapidly became a realization in the US (February 2020), the utilization of cancer screening procedures (colonoscopy, mammography, CT scans, pap smears etc.) were observed to significantly decline. Overall, nationally in the US a 60-80% decrease in cancer screening was recorded. (Cancino et al., 2020) (Van Haren et al., 2020) One study, evaluating claims data reported 87% reduction in mammograms, 83% reduction in pap smears and a 90% decrease in colonoscopies by early April 2020. (Mitchell, 2020) This delay in screening is undoubtedly going to have a major impact in the overall effect on cancer morbidity and mortality. In fact, the overall effects of delays in cancer screening nationally are already started to surface. It is estimated that over 22 million Americans will be compromised if testing for cancer screening remain at the low levels observed at the height of pandemic. This means that approximately 80,000 positive cancer cases can be expected to have a delay in their diagnosis. (Yong et al., 2020) (Bakouny et al., 2020) Sadly, delayed diagnosis of cancer in some of these cases may mean a lost opportunity for cure, while for many others it will result in upstaging of cancer and higher morbidity. (Giesen et al., 2020) (Pathania et al., 2021) Thus, COVID-19 is not only directly lethal to the patients, but also has the potential to indirectly amplify its mortal impact through suspension of the cancer screening services. As the US cautiously disengage from "social distancing", healthcare services are also testing waters to ramp up services for their patients. Thus, a steady recovery in cancer screening practices is fortunately anticipated. There remains significant ambiguity as to what is the best practice for reinstatement of these programs in the post-COVID era, which has yet to realize. However, it is clear that as the duration of this pandemic has extended significantly beyond the initial reported assessments, the need to reinstate cancer screening programs to at least the pre-COVID momentum is an undeniable priority.

Serum Potassium Levels and Adverse Outcomes in Patients with Acute Myocardial Infarction

Rizwan Abbas,¹ Tazeen Nazar,² Bilal Aziz,³ Furqan Saeed,⁴ Kashif Nawaz,⁵ Muhammad Nabeel⁶

Abstract

Objective: To determine the effect of serum potassium levels on short term mortality outcomes in patients with acute myocardial infarction.

Methods: This Descriptive Case Series was conducted in the CCU of Mayo Hospital Lahore from 15th November, 2017 to 15th May, 2018. A total of 156 patients of either sex between the age group of 30-60 years and diagnosed as cases of myocardial infarction with symptoms of less than 24 hours duration and serum potassium level of <3.5 mEq/L were included in the study. Patients were then followed up for 7 days and adverse outcome was recorded. Data was analyzed using computer software SPSS Version 22.0.

Results: Out of the 156 patients, 119 (76.3%) were males and 37 (23.7%) were females. Mean age of the patients was 47.88±6.24 years, mean weight 85.31±13.14 Kg, mean duration of presenting complaints was 10.269±4.51 hours and mean Serum Potassium levels were 3.05±0.25 mEq/L. Adverse outcome in the form of mortality due to arrhythmias was seen in 15 (9.6%) patients.

Conclusion: Low serum potassium level (<3.5mEq/L/L) was significantly associated with increased adverse outcome in acute myocardial infarction patients.

Keywords: Acute myocardial infarction, Low serum potassium levels, Adverse outcome

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Introduction

Potassium homeostasis is vital in preventing adverse effects in patients having cardiovascular disease. Numerous studies have shown an association of low levels of serum potassium, frequently less than 3.5 mEq/L, with the risk of having ventricular arrhythmias in acute myocardial infarction (AMI) patients.¹ Two neurohormonal mechanisms have been proved to play a key role in AMI: the renin – angiotensin–aldosterone system and the adrenergic autonomic nervous system.¹ Damage to the myocardium, systolic or diastolic dysfunction, peripheral hypoperfusion and hypertension of pulmonary veins all contribute to

activation of neurohormonal response that maintains homeostasis and also contributes to further injury. Serum potassium levels are maintained in humans in the 3.5 to 5.0 mEq/L range at organ, cellular and molecular levels. Neurohormonal response changes that occur in AMI are depicted in the serum potassium levels and response of the body in maintaining a normal range.²

Hypoperfusion of the kidneys and vasoconstriction at the pre-glomerular level contributes to a decreased glomerular filtration thereby leading to potassium retention and hyperkalemia. Aldosterone release favours hypokalemia through reabsorption of sodium and exchange of potassium. Krogager et al. followed cases registered with the Danish health services and investigated the relationship between serum potassium levels taken at seven different defined intervals and deaths attributed to any cause within ninety days in patients after an AMI.³ The survival analysis of the patients were based on the first measurement of serum potassium and in order to reduce bias, day 0 i.e., the day of presentation and day 1 were eliminated.

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As expected, levels of serum potassium not falling within the reference range were associated with higher risk of death and depicted through a specific U-shaped curve. This finding was not unfamiliar in patients with AMI.^{4,6} This report was subjected to multi-variate analysis and the findings reinforced the association of potassium levels falling in the range of 3.5–3.8 mEq/L (HR: 1.82; 95% CI: 1.21–2.74) and 4.5–5.0 mEq/L (HR: 1.54; 95% CI: 1.08–1.21) and an elevated death risk when compared with potassium levels in the 3.9–4.5 mEq/L range.

A study by Goyal A, et al. has shown that frequency of mortality was 11.4% in patients with low serum potassium levels with acute myocardial infarction.⁷

In another study by Uluganyan M, et al., the frequency of mortality was 2.4% in patients with low serum potassium levels with acute myocardial infarction.⁸

The recent guidelines recommend to maintain a serum potassium level of >4-4.5 mEq/L in AMI patients.^b On the contrary, some clinical trials carried out recently have shown an increased death rate with serum potassium level of >4-4.5 mEq/L.^{4,7} The aim of this study is to determine the effect of serum potassium levels on short term mortality of patients with acute myocardial infarction in our general population. This study will pave the way for further research in this field and will help to understand impact of low potassium levels on mortality rate in our general population.

Methods

This Descriptive Case Series was conducted in the Coronary Care Unit (CCU) of Mayo Hospital Lahore from 15th November 2017 to 15th May 2018. A sample size of 156 cases was taken using 95% confidence level, 5% margin of error and taking expected frequency of adverse outcome in the form of mortality as 11.4%.⁷ Non-Probability Consecutive Sampling Technique was applied in selection of the cases. Patients of either gender between the age group of 30-60 years with the diagnosis of Myocardial Infarction as per operational definition and presentation to the hospital within 24 hours of onset of symptoms and having serum potassium level of <3.5 mEq/L by laboratory test at the time of presentation were included in the study. Patients with the history of heart failure, renal failure defined by serum creatinine of >2.2 mg/dl on laboratory test, presentation to the hospital more than 24 hours after the onset of symptoms and history of coronary artery bypass grafting

were excluded from the study.

After approval from the Board of Studies (BOS) and Institutional Review Board (IRB) of King Edward Medical University, Mayo Hospital, Lahore, all patients conforming to the inclusion criteria were enrolled in the study. Written informed consent ensuring confidentiality and safety was taken from all the selected patients. Baseline demographic information of patients (age, gender, weight and duration of complaints) was taken. Baseline echocardiogram (ECG), serum troponin T and potassium levels were done. Patients were then followed up for the next 7 days and adverse outcome in the form of mortality was noted and recorded on a pre-designed proforma.

Data was analyzed using computer software SPSS version 22.0. Quantitative variables like age, serum potassium levels, duration of complaints and weight were presented as Mean±SD. Qualitative variables like age, gender and adverse outcome were presented in the form of frequency and percentages. Effect modifiers like age, gender, serum potassium levels, duration of complaints and weight were controlled by stratification. Post stratification chi-square test was applied and p-value of ≤ 0.05 was considered statistically significant.

Results

The mean age of the patients was calculated to be 47.88 ± 6.24 years, mean weight was 85.31 ± 13.14 Kg, mean duration of complaints was 10.26 ± 4.51 hours and mean Serum Potassium levels were 3.05 ± 0.25 mEq/L. Majority of the patients were in the age group of 46-60 years i.e., 102 (65.4%) compared to 54 (34.6%) patients in the 30-45 years age group. There was a male gender predominance i.e., 119 (76.3%) compared to 37 (23.7%) females. Adverse outcomes in the form of mortality due to arrhythmias were seen in 15 (9.6%) patients only. Stratification of adverse outcome with respect to age, gender, weight, duration of complaint and serum potassium levels are shown in Table-1-3 respectively.

Discussion

The results of this study showed that admission serum potassium level of <3.0 mEq/L was associated with increased adverse outcome in patients with acute myocardial infarction. Hypokalemia i.e., serum potassium levels < 3.5mEq/L in patients with acute myocardial infarction is primarily accredited to catechola-

mine surge.¹⁰ Catecholamines stimulate Na-K-ATPase pump and shift K⁺ intracellularly, thereby leading to redistributional hypokalemia. This results in hypopolarization of the viable, non-ischemic myocardial

Table 1: Stratification of Adverse Outcome with Respect to Age, Gender and Weight

Parameters	Adverse outcome		P value	
	Yes	No		
Age	30-45 years	6(11.1%)	48(88.9%)	0.645
	46-60 years	9(8.8%)	93(91.2%)	
	Total	15(9.6%)	141(90.4%)	
Gender	Male	11(9.2%)	108(90.8%)	0.778
	Female	4(10.8%)	33(89.2%)	
	Total	15(9.6%)	141(90.4%)	
Weight	≤70kg	2(5.4%)	35(94.6%)	0.320
	>70kg	13(10.9%)	106(89.1%)	
	Total	15(9.6%)	141(90.4%)	

Table 2: Stratification of adverse outcome with respect to duration of complaints

Duration of complaint (hours)	Adverse outcome		P value
	Yes	No	
1-12	3(2.8%)	104(97.2%)	0.000
13-23	12(24.5%)	37(75.5%)	
Total	15(9.6%)	141(90.4%)	

Table 3: Stratification of adverse outcome with respect to serum potassium levels

Serum potassium levels (mEq/L)	Adverse outcome		P value
	Yes	No	
<3.0	10(21.7%)	36(78.3%)	0.001
3.0-3.4	5(4.5%)	105(95.5%)	
Total	15(9.6%)	141(90.4%)	

tissue and electrical non-homogeneity responsible for causing ventricular arrhythmias. Previous studies have shown a high incidence of ventricular arrhythmia within a few days following MI and associated it with hypokalemia.¹¹ Although most of these studies were carried out during the time when modern treatment options like beta-blocker and early reperfusion therapy were not available. So guidelines were formulated to maintain a serum K⁺ level of >4-4.5 mEq/L in patients following acute MI.^{12,13} Beta-blockers cause an increase serum potassium level and suppress ventricular arrhythmias by depressing K⁺ levels induced through catecholamine surge. Beta-2 receptors inhibit the Na⁺-K⁺-ATPase pump and contribute to the catecholamine surge.¹⁴ Studies have shown that if beta blockers are administered early in the post

STEMI period, then a decreased incidence of ventricular arrhythmias, sudden cardiac death and mortality were observed.^{15,16}

A study conducted by Goyal A et al showed 11.4% mortality in patients with low serum potassium levels following acute myocardial infarction.⁷ However, a study performed by Goyal et al.⁷ on a larger population, surprisingly related a mean serum K⁺ level above 4.5 mEq/L to be associated with increased mortality. This led to a suggestion that in patients with AMI, serum K⁺ level should be optimized within the 3.5 and 4.5 mEq/L range.⁷ This proposal posed a challenge to the guidelines recommended for K⁺ level. Recently a study carried out by Choi and colleagues⁴ supported the findings of Goyal et al.⁷ They proved mean serum K⁺ level of >4.5 mEq/L to be associated with increased hospital and delayed mortality.⁴ Although beta blockers and angiotensin-converting enzyme inhibitors were not used often for the treatment of high potassium levels >4.5mEq/L in that study, it was still associated with higher long-term deaths.⁴ Even though our study took serum K⁺ level at the time of admission rather than taking mean K⁺, it showed congruity with Choi and Goyle studies.

This finding was facilitated by Choi and colleagues.⁴ A possible explanation could be low K⁺ levels responsible for compromising myocardial contractility and relaxation mainly due to high levels of vasopressors.¹⁷ Some degree of insulin resistance was also observed during the early period following AMI.¹⁸

In another study by Uluganyan M, et al., the mortality was 2.4% in patients with low serum potassium levels with acute myocardial infarction.⁸

There are certain limitations in this study. Being observational, and despite using newer and sturdy methods with statistical analyses, a possibility of residual confounding still exists, i.e serum potassium level and untoward events may be linked reversely. Specifically, the high Odds Ratio for mortality at low potassium levels (<3.0) are only based on limited events, are likely to be affected by outliers and rather than showing a causal relationship, may be attributed to severe illness. So large clinical trials showed be carried out targeting different K⁺ levels in patients with AMI so as to define the optimal range. Ahead of large trials, based on the findings of our study, we would not recommend very aggressive treatment of low K⁺ levels in the 3.5 to 3.9mEq/L range as levels of <4.5mEq/L may not be very harmful.. Our study was conducted only in patients with AMI so these reference values may not be applicable in patients

with other cardiac conditions e.g., congestive cardiac failure. Lately, a trial conducted on congestive cardiac failure patients documented an increased death rate in patients having serum K⁺ levels less than 4.0 mEq/L, but β-blockers known for causing high potassium levels and lowering mortality rates were not used in that study.¹⁹ We recommend studies similar to ours to be conducted in patients with congestive cardiac failure and a consensus development on serum K⁺ levels with the aim to reduce mortality in these patients.

Conclusion

We concluded that admission serum potassium level was significantly associated with increased adverse outcome in patients with acute myocardial infarction. A low serum potassium level i.e., <3.0mEq/L was associated with higher mortality.

Conflict of Interest: None

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Authors Contribution

RA, TN: Conception/ization of Project
RA, BA, FS, MN : Data Collection
TN, BA, KN: Literature Research
KN, MN: Statistical Analysis
RA, TN, FS: Drafting, Revision
TA, BA: Writing of Manuscript

Hand's Functional Status of Children with Rheumatoid Arthritis in Everyday Activities: A Cross-Sectional Study

Hafiza Ayesha Ikram,¹ Wajeעה Abdul Ahad,² Fazila Huma³

Abstract

Objective: Rheumatoid Arthritis [RA] is a chronic, systemic, autoimmune disease on an unknown aetiology. It leads to the progressive destruction of joints. It also warrants difficulties in performance of Activities of Daily Living (ADL). This study aimed at determine relationship between activities of daily living [ADL] and functional status of the hand.

Methods: This Crosssectional Study was conducted at Romatology Department Children Hospital and Sheikh Zayed Hospital Lahore from June 2018 to December 2018. Convenient sampling technique helped in the collection of data. A hand function questionnaire and the Barthel Index were the contributory data collection methods. Rheumatoid Arthritis [RA] patients selected were those experiencing functional impairment in hands, having difficulty in performing ADL.

Results: The patients who were able to perform the hand function test were independent in their daily life activities. Whereas, those who were not able to perk the test were dependent on their daily life activities.

Conclusion: It was found that children with RA had a significant association between performing the ADL and functional status of hand.

Key Words: Activities of Daily Living [ADL], Rheumatoid Arthritis [RA]

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Introduction

RA is a systematic and chronic disease of inflammation of not-known aetiology, which affects joints in a symmetrical fashion causing painful swelling and deformity. Rheumatoid arthritis [RA] leads to progressive destruction of joints and difficulties in performing daily living activities. This leads to Synovial Membrane inflammation that causes highly cellular inflammatory Pannus tissue's formation. The Pannus grows over infiltrating ligaments, cartilage, and tendons, resulting in erosion of the cartilage and of the subchondral bone, along with disruption of the ligamentous insertions, and impairment of tendon

glide.¹ There may be variation in its clinical presentation. It may be a mild and self-limiting arthritis or a harsh multisystem inflammation, this too with more than necessary articular manifestations. For majority of patients, hand involvement is typically present. But it causes motion limitation, deformity or weakness, stiffness in the morning, swelling, and pain. Such impairments can trigger deterioration of the hand functions and hinder ADL.

RA affects the hand in several ways. In fingers, it can cause Boutonniere deformity, Swan-neck deformity, Trigger fingers, Tendon rupture, and Opera glass hand. While in thumbs, it causes Type 1 to Type 6 thumb deformities. In Wrists, it can cause the De Quervain's Tenosynovitis and "Zigzag" deformity.² As for Metacarpophalangeal joint, it causes Volar subluxation and Ulnar deviation. Reduced grip strength, pain, and these deformities have a crucial impact on hand functioning and performing activities of daily living [ADL]. According to occupational therapy, Activities of daily living [ADL] are the basic tasks or

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activities that can help a person to qualify as someone who is able to maintain everyday independence. These activities are Eating, Drinking, Grooming, Bathing, Dressing, Toileting, Transferring and Mobility. Rheumatoid Arthritis [RA] affects hand functioning and leads to dependency. There are a number of factors for the impairment of the handgrip strength in a patient with RA. Because of swelling of hand, the pain, the active inflammation, the ability of the hand to apply force is affected and become diminished. The Flexor Tendon Gliding may become impaired by the Wrist Tenosynovitis. Having this impairment affects the strength applied by the long flexor muscles of the fingers, significantly reducing it. And using force to grasp a thin or a narrow handle is further complicated by the loss of finger flexion owing to contractions. Pain becomes the norm and other difficulties are developed by this decreased grip strength and hand dexterity when performing activities of daily living [ADL].

Methods

This study is of cross-sectional nature. Developing or establishing a correlation between activities of daily living [ADL] and the functioning of hand is the hypothesis of this study. The hypothesis was that hand functioning and activities of daily livings [ADL] are deeply correlated. The sampling frame consisted of 59 patients. Convenience sampling technique helped in the selection of these patients. Out of 59 patients, 61% were female, while 39% were male. The inclusion criterion for the RA patients is that they must be 5 to 16 years of age. Anyone unable to fulfil this criterion will not be a participant in this study. Out of 59 patients, 42.37% of patients were in the age range 6-10 years, while the rest were in the age range 11-16 years. This study took place over a duration of 6 months, spanning from June 2018 to December 2018. Data collection done at the Department of Rheumatology Children Hospital & ICH, Lahore and Sheikh Zaid Hospital, Lahore. Collection of data is through standardised proforma; Hand Functional Index and Barthel Index. Data of Rheumatoid Arthritis [RA] patients were collected by inquiring them as per the proforma. Statistical Package for Social Sciences (SPSS) version 24 will be used for data analysis. To find the functional status of hand and its impact on daily life activities, descriptive analysis and chi-square test will be used. This study aims to prove that

the increase in joint mobility limitation and disease activity increases the risk of functional disability.

Result

For grooming in relation with a thumb tip, 27% performed the test with no delay, with 94% (of those with no lag) being independent, whereas, of those who delayed, 34% were independent. 39% did not perform test fully and required help in grooming. For grooming in relation with 2nd finger, with no delay, 27% were independent in grooming, whereas, 37% of those who delayed were independent. However, 35% were not able to perform the test and required assistance in grooming. For feeding in connection with bending of 3rd finger, 28% of successful were self-sufficient. Whereas 35% of somewhat successful were independent, and 29% were somewhat dependent, while 14% were utterly dependent. 35% were unsuccessful, out of which 18% were unable to feed, and 3% depended on others. For usage of a toilet in connection with bending of 4th finger, 17% of the successful were self-sufficient. 32% were unsuccessful, out of which 58% were independent, 31% needed some help, and 11% utterly dependent on others. For dressing in connection with bending of 5th finger, 28% of the normally expected performed tests were self-sufficient. 34%, of those who did not fully bend their finger, were independent in dressing, whereas, 37% of those whose fingertip did not reach palm were dependent in dressing.

For grooming in relation with the antebrachium held horizontal, palmer surface pressed together point upward, 32% of the performed tests were with no delay. 18 out of 19(32%) were independent in grooming. 45%, of the performed tests, were with delay, out of which 14 were self-sufficient, whereas 13 required help. For toilet usage in relation with the antebrachium held horizontal, dorsal surfaces pressed downward, 28% of the performed tests with no delay were independent. For feeding in connection with the elbow held rectangularly: ulnar margin of hand lifted and both back of the hands placed on the table simultaneously, 28% of the performed tests with no delay were independent. 35% were unable to finish the test properly out of which 3 needed help, whereas 18 were unable to feed. For grooming concerning the radial margins of hands simultaneously placed on the table: thumbs point downward, 27% were self-sufficient. 40% had planes of hand perpendicular. 15(58%)

out of 26 (40%) were independent in grooming, whereas 11(42%) required help. For bathing concerning the radial margins of hands simultaneously placed on the table: thumbs point downward, 27% were able to perform the test and were self-sufficient. However, 28% were unable to show the hand function and they were dependent. All recorded values were less than 0.005%, showing significance. There is an association between a correlation between ADL and hand functioning.

Moreover, it had affirmed that the Occupational Therapy Motor had the following roles:

1. Maintaining or increasing the range of motion and mobility of joints.
2. Maintaining or increasing the strength of muscle.
3. Maintain or improve endurance.
4. Maintain or improve functional ability.
5. Prevent or correct joint deformity, make and keep the patient personally independent.
6. Consider a splint to prevent ulnar deviation deformity of the hand and the wrist.
7. Consider splints to maintain wrist extension of the hand.

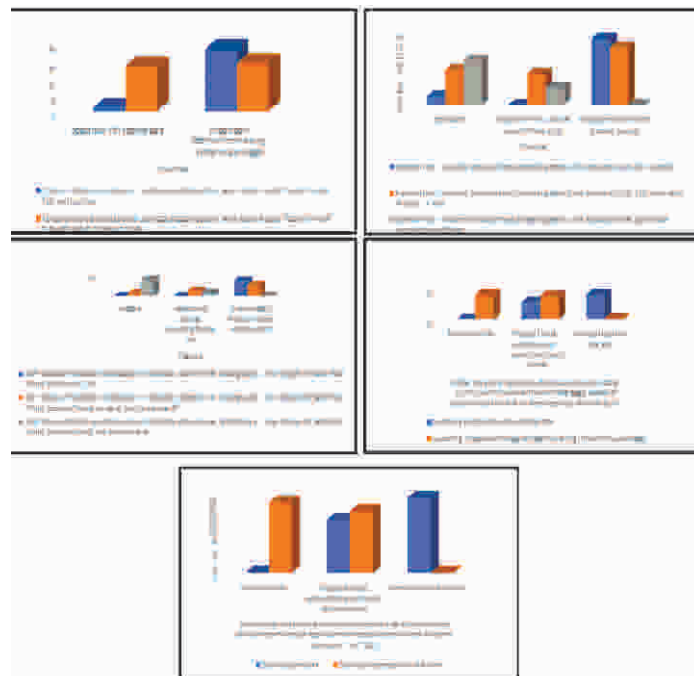
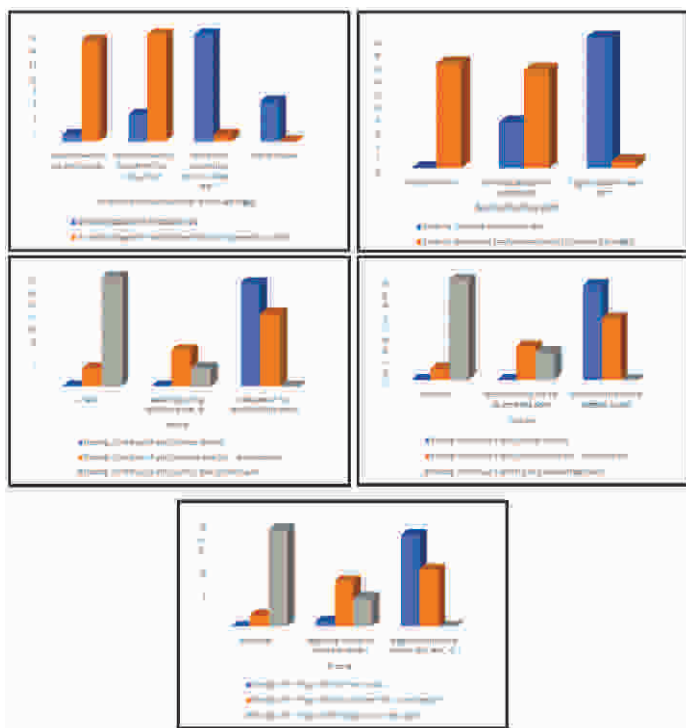


Table 1:

Inferential Analysis				
	5th finger	Chi-Square	df	P-value
Grooming	2nd finger	38.538	3	0
Grooming	3rd finger	35.934	2	0
Feeding	4th finger	48.136	4	0
Toilet use	5th finger	48.411	4	0
Dressing	Forearm	46.454	4	0
Grooming		28.025	2	0
Toilet use	Lift ulnar margin	25.631	4	0
Feeding	Radial margin	48.136	4	0
Grooming		39.261	4	0
Bathing		29.64	2	0

Discussion

Rheumatoid Arthritis, commonly abbreviated as RA, is a systemic and chronic autoimmune illness of not-known aetiology, and also chronic, that leads to the destruction of joints progressively, affecting joints in a symmetrical fashion causing painful swelling and deformity. It also hinders the performance of ADL. It causes inflammation of the Synovial Membrane, which leads to the formation of highly cellular inflammatory pannus tissue. Developing or establishing a correlation between ADL and hand functioning for patients with RA is the aim of this study. Bjelle conducted research spanning a period of five years. His research was about the capacity of activists of daily living [ADL] and how it related to the functioning of the hand for patients with Rheumatoid Arthritis [RA].³ In this study, the number of patients included was 43, out of which 28 were males, whereas there



were 15 females, and the mean age of all participants was 53.7 years. 7.5 years was the calculated duration for which the patients have had the disease. Many factors, that were measured, contributed to the results. These were the K-function Test [KFT], the Grip Ability Test [GAT], self-estimated hand function, the Health Assessment Questionnaire [HAQ], grip strength, and pain scales. The results of three Health Assessment Questionnaire [HAQ] components, the Grip Ability Test [GAT], and the K-function Test [KFT] were quite significantly worse for female patients, as compared to male patients. So, in our research, the number of females was higher as compared to males.

Palmar et al. conducted a study to investigate the handgrip strength and its relation with hand dexterity in patients with Rheumatoid Arthritis [RA].⁴ The participants were 32 women of 18 - 70 years. Using the Handgrip strength, pinch strength, the Purdue Pegboard test, this study focused on patients with RA in order to determine clinical relevance, if any, of rapid disabilities of hand, shoulder, or arm and dexterity of hand, and as to how they are interrelated to each other. This study concluded that strength of handgrip was related to disability and activity of disease in RA patients. Erol Am et al. studied Rheumatoid Arthritis [RA] and how it affects the functional status of hand.¹ There were a total of 38 patients and 33 controls in this study. Purdue Pegboard Test [PPT] helped in assessing coordination and dexterity. The Durouoz Hand Index [DHI] helped in assessing hand disability. This study concluded that Rheumatoid Arthritis [RA] had a negative impact on hand function. Gizemirem Kinikli et al. studied functional disability of upper extremity and strength of grip of patients with RA.⁵ The study consisted of 29 patients and used The Durouoz Hand Index [DHI] for assessing hand disability. Stanford Health Assessment Questionnaire [SHAQ] was used for measuring physical disability. The study concluded that strength of lower handgrip and its endurance were related to functional disability of upper extremity in RA patients. The validity of the hand QUICKDASH questionnaire and the disabilities of the arm and shoulder were researched by Kensuke Ochi et al. They employed patients with Rheumatoid Arthritis having functional impairment for this study. This study consisted of 94 patients.⁶ The result showed that QUICKDASH, for evaluating impairment of upper extremity, index of

disability and control of disease in a large cohort of RA patients was suitable. Some researchers researched the relation between the handgrip, pinch strength and activity of disease (impairment of functions in patients with RA). Dynamometer helped in assessing handgrip. Analysis of these relations was done with the help of the Signals of Functional Impairment [SOFI], the Health Assessment Questionnaire [HAQ], and the Durouoz Hand Index [DHI]. A negative correlation between activity of the disease, includes impairment of functions, disability and the duration of the disease, and strength of handgrip and strength of pinch of patients with Rheumatoid Arthritis [RA]. Kenrir, Nampei et al. studied the association between pinch strength and hand dysfunction, finger deformities, and contact points.⁷ Eighty-four hands of forty-two patients with Rheumatoid Arthritis [RA] were evaluated by them. They determined functional status using the Hand Disability Index [HDI] and found a correlation between pinch strengths and hand disability. Rheumatoid Arthritis [RA] patients' disability of arm and shoulder [DAS] was researched by Aktekin LA et al.⁸ This study comprised of 166 patients. Hand questionnaire, Health Assessment Questionnaire [HAQ], and DASH helped in assessing the relationship with activity of disease. DASH score was statistically high with increased activity of the disease. DASH and HAQ displayed a correlation ($r=0.883$). In order to research or study the relationship between the disease activity and the hand functioning of patients with Rheumatoid Arthritis [RA], the short-form score for the assessment and quantification of chronic rheumatoid affections of the hands, or SF-SACRAH, was employed by Singh H et al.⁹ There were 100 patients included in the study. It was discovered in the study that, as per the assessment of DAS-28 scores, the activity of disease for patients with RA had a weak correlation with hand functions. This was especially true for the remission states and the low activity of the disease. The hand functions were assessed as per the M-SACRAH and the SF-SACRAH, and both were quite significantly correlated. Therefore, assessing of Rheumatoid Arthritis [RA] patients by SF-SACRAH was suggested. A study on grip strength, activities of daily living [ADL], hand functioning, and some essential assistive devices was published by Shipham & Pitout.¹⁰ They concluded that the loss of strength of the grip is the principal pointer for assistive devices. The usage of assistive

instruments increased and Activities of Daily Living (ADL) became more difficult as the grip became weak. Their result showed the highest correlation between grip strength and Activities of Daily Living (ADL). Our study had revealed similar results for Rheumatoid Arthritis (RA) patients. We also observed a very high correlation between hand functioning and Activities of Daily Living (ADL). Carol A. Kennedy et al. conducted a study on properties of the measurement of the QUICKDASH (Disabilities of the Arm, Shoulder and Hand), measure of outcome and adaption of cross-cultural QUICKDASH.¹¹ An acceptable performance of the tool was observed in this study. This was backed by strong evidence of validity and reliability through hypothesis testing. For structural validity testing, there was also moderate and positive evidence. Mathilda A Björk et al. conducted a study on hand function and activity limitation in rheumatoid arthritis.¹² Signals of Functional Impairment [SOFI] and the Grip Ability Test [GAT] helped assess the hand function. Grippit helped in the measurement of grip force. The Swedish version of the Health Assessment Questionnaire [HAQ] helped assess activity limitation. As compared with healthy referents, GAT, grip force, SOFI-hand, and HAQ were significantly different for the patients of both sexes throughout the study. In Rheumatoid Arthritis [RA] patients, HAQ had a link with grip force, whereas in healthy referents, it had a link with age and GAT. López López CO1 et al. conducted a study on Hand function in rheumatic diseases.¹³ Their study included 40 patients (72% women and mean age of 49.25 ± 14.2 years) and used m-SACRAH and the Health Assessment Questionnaire Disability Index [HAQ-DI]. Although there was only a correlation with limited motion joints, a good correlation was discovered for a patients' perspective variables. For the limited motion joint, the value for "r" was equal to 0.41 and "P" was less than 0.05 in M-SACRAH, whereas in HAQ-DI merit of "r" equalled 0.03 and for "P" was less than 0.05. For patients' perspective variables, the merit of "r" equalled 0.43 and for "P" was less than 0.05 for both M-SARAH and HAQ-DI. In our study, the result showed that patients with Rheumatoid Arthritis (RA) had a good relationship between hand function and activities of daily living (hand function / Barthel: $P < 0.05$). In order to prevent harsh or severe deformities, finger flexor muscles' and wrist's strengthening exercises were crucial, as per the study of Stephanie

Robinson Cima et al.¹⁴ Some of the functions lost owing to the progression of the disease were also re-established with the help of these exercises.

Conclusion

This study aimed to reveal how patients with Rheumatoid Arthritis (RA), with an object quality of life, suffered from a functional disability. The data were collected only from 2 institutes and comprised of only fifty nine patients. As these were minors, their caregivers were present or interviewed on their behalf. Some caregivers were quite non-cooperative. However, these results suggest that the certified caregiver should also be attentive towards the grip strength of the patients, as well as to measure the mobility of their joint, in order to develop or create such strategies that can improve the physical functioning of patients with Rheumatoid Arthritis (AR). However an observation made was that the function of hand and difficulty in ADL, correlated in Rheumatoid Arthritis (RA) patients with less hand function indication more struggle in daily life activities.

Conflict of Interest: None

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Authors Contribution

IAH: Conceptionlization of Project, Writing of Manuscript

HF: Data Collection

IAH, HF: Literature Search

AAW: Statistical Analysis, Drafting, Revision

RA, TN, FS: Drafting, Revision

Comparing SSI In Purse-String Versus Conventional Primary Closure Following Stoma Reversal

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Abstract

Objective: To compare the frequency of Surgical Site Infection (SSI) and mean length of hospital stay between the Purse-string closure and conventional primary closure techniques for stoma reversal.

Methods: The study was carried out in Surgical Unit-III, Lahore General Hospital Lahore from January 5, 2018 to July 5, 2018. The study designed as a Observational Study. Patients undergoing surgery for Ileostomy were randomly divided into two groups, Group-A (Purse-string closure) and Group-B (Conventional primary closure). All the patients were called for follow up checkup on 14th days after operation and after one month. Both of the groups were checked and recorded for SSI after operation and hospital stay. The data was statistically analyzed by using SPSS v23.0.t test (independent sample) used for the comparison of hospital stay mean. Chi-square was also used for the comparison of the frequencies of SSI. Data were stratified for gender and age. A p-value ≤ 0.05 was considered as significant.

Results: A total of 140 patients were enrolled for this study. Patients were divided into two groups i.e. Group-A (Purse-string closure) and Group-B (Conventional primary closure). In group-A, mean duration of hospital stay was 5.7 ± 1.0 days, while 7.3 ± 1.1 days in group-B, which is statistically significant with a p-value of 0.000. In group-A, surgical site infection was in 4(5.7%) patients, while 11(15.7%) patients of group-B, which is statistically significant with a p-value of 0.046.

Conclusion: The frequency of surgical site infection and mean length of hospital stay after stoma reversal, purse-string suturing technique is significantly less than conventional primary closure technique.

Key Words: Surgical stoma; Ileostomy; Closure; Infection.

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Introduction

In colorectal surgery it is properly known that anastomotic leakage is an main problem and complication, specially in coloanal anastomosis and low colorectal. The momentary defunctioning stoma may decrease the re operative rate and anastomotic

leakage.¹⁻²

The surgery of stoma reversal is generally done when the general conditions of medical recovers in patient. The surgery of stoma reversal might be caused the morbidities and complications like SSI (surgical site infection), postoperative ileus paralytic, bowel obstruction, anastomotic dehiscence and fistulas enterocutaneous.³⁻⁵

The Surgical Site Infection is a very common and important morbidities that wound contamination at site is difficult to preventable. In past CPC (conventional primary closure) technique is the common method that used for the closure of skin in the surgery of stoma reversal with reported results that ranging from 3% to 43%.⁶⁻⁷ SSI after following stoma reversal increase the wound risk of incisional hernia, dehiscence,⁸ health care costs and hospital stay length.⁹

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To stop Surgical Site Infection after stoma reversal many techniques used that developed like implementation of gentamycin sponge subcutaneous, iodine wound irrigation, closing of wound by drain tube, late primary closure, secondary closure and string purse closure.¹⁰⁻¹¹

In 1997, Banargee¹² firstly reported a reliable, simple and cosmetically useful method of skin closure called as PSC (purse string closure). PSC method gives a small opening for the drainage of discharge of wound. This method also heal the wound rapidly than other method of wound healing or wound closure like primary delayed and secondary wound closure techniques.

In a study, it was concluded that, Surgical Site Infection was 36.67% in primary closure and 10% in Purse-string closure group.¹³ In another study, it was reported that, Surgical Site Infection occurred in 15.7% and was more frequent in the Primary Closure group than in the Purse-string closure group 21.4% vs. 10%. Time of hospital stay in the Purse-string closure group was shorter than it was in the Primary Closure group (14.79 days vs. 16.44 days).¹⁴ In another study, it was found that infection occurred in Purse-string closure patients 2.9% and in Primary Closure patients 21.8%. Time of hospital stay in the Purse-string closure group was shorter than it was in the Primary Closure group (6.55 days vs. 6.78 days).¹⁵

Hypothesis

There is difference in Purse-string closure versus conventional primary closure in terms of less Surgical Site Infection and hospital stay for stoma reversal.

Methods

This Observational Study was conducted in Surgical Unit-III, Lahore General Hospital, Lahore. From January 5, 2018 to July 5, 2018. Patients were sampled via Non probability consecutive sampling. The sample size of 140 (70 in each group) cases was estimated by using 95% confidence level, 80% power of test with an expected percentage of surgical site infection in both groups with Purse-string closure 2.9% and conventional primary closure 21.8%.¹⁵ Surgical Site infection was defined as southampton grade IV and V.

Following patients were included in the study 1. Patients of both gender 2. Patients ages between 25-70 3. Patients undergoing surgery for having ileosto-

my for benign disease of intestine (as per operational definitions).

Following patients were excluded 1. Patients with pre-existing stomal site wound infection 2. Reversal of stoma through laparotomy 3. Post-operative anastomotic leak 4. Uremic patients 5. Patients on chemotherapy and radiations

After taking written informed consent, patients undergoing surgery for Ileostomy were randomly divided into two groups by computer generated lottery method, Group-A (Purse-string closure) and Group-B (Conventional primary closure). All operations were done by same surgical team.

In group A and B following method used like in A for the ileostomy reversal circular incision used with stitches of continuous and non-absorbable. The wound of skin was closed by using (Prolene No. 1) that leaving 0.5 cm defect on middle in the skin. In B for the ileostomy conventional incision used. Skin approximately resulting in linear scar.

When these assessments were made the patient were still admitted in hospital. Then all the patients were called for follow up checkup on 14th days after operation and after one month. Both of the groups were checked and recorded for SSI after operation and hospital stay. All surgeries were done by the same surgical team to reduce bias. All the data and information were collected by proforma. The data was statistically analyzed by using SPSS v23.0. For the quantitative variables like age, hospital stay length mean and standard deviation were calculated. For qualitative variable like gender and SSI the frequency distribution and percentages were calculated. t test (independent sample) used for the comparison of hospital stay mean. Chi-square was also used for the comparison of the frequencies of SSI. Data were stratified for gender and age. Respective tests of significance were applied post stratification. p-value ≤ 0.05 was considered as significant.

Results

A total of 140 patients were enrolled for this study. Patients were divided into two groups i.e. Group-A (Purse-string closure) and Group-B (Conventional primary closure). In group-A, there were 41(58.6%) males and 29(41.4%) females, while in group-B, there were 39(55.7%) males and 31(44.3%) females. Mean age of group-A patients was 50.9 \pm 14.4 years

and 45.5 ± 12.8 years in group-B. In group-A, 18(25.7%) patients were in 25-40 years age group, while 20(28.6%) and 32(45.7%) were in 41-55 years and >55 years age groups respectively. In group-B, 28(40.0%) patients were in 25-40 years age group, while 25(35.7%) and 17(24.3%) were in 41-55 years and >55 years age groups respectively. In group-A, 26(37.1%) had normal weight, while 23(32.9%) and 21(30.0%) were overweight and obese respectively. In group-B, 21(30.0%) had normal weight, while 24(34.3%) and 25(35.7%) were overweight and obese respectively. In group-A, mean duration of hospital stay was 5.7 ± 1.0 days, while 7.3 ± 1.1 days in group-B, which is statistically significant with a p-value of 0.000. In group-A, surgical site infection was in 4(5.7%) patients, while 11(15.7%) patients of group-B, which is statistically significant with a p-value of 0.046.

Discussion

In this study significant results were found that a lower rate of SSI linked with PSC (purse string closure) when compared with CPC (conventional primary closure (CPC)) (5.7% vs. 15.7%, $P = 0.046$).

Our study results matched with two other recent studies that were also small and randomized controlled trials.¹⁶⁻¹⁷ Compared the PSC and CPC after stoma reversal. Reid et al. randomly allotted 61 ileostomy patients to either CPC and PSC and found a significant lower rate in Surgical Site Infection than PSC group (6.7% vs. 38.7%, $P = 0.005$).¹⁸

The estimated sample size of study was 60 patients and 66 was enrolled. The trial halted due to the overwhelming number in SSI than CPC group.

Camacho-Maurieset al.¹⁶ assigned randomly 61 patients with colostomies or ileostomies to CPC or PSC group. They find nil SSIs in PSC group as compared with other group with 36.6% SSI rate in the CPC group ($P < 0.0001$).¹⁷

The estimates of sample size or the rates of SSI were not reported that used in the calculations. Surgical Site Infection rates in CPC group for both above mentioned studies were reported highest for this technique.¹⁹

In present study the rate of Surgical Site Infection i.e. 15.7% in CPC group lies in middle range of previous studies reports^{18,20-21} with proper sample size and analysis of multivariate to handle potential confounders.

Our study also confirms the SSI rate in stoma site is

more in CPC group than PSC group. Our results may be generalizable for all patients who undergo colostomy reversals or ileostomy.

The data of this study also matched with previously mentioned studies that includes controlled randomized trials also as other retrospective reviews and case control studies.²²⁻²³

In our study, all stoma Surgical Site Infection were managed bedside by opening the incision to allow the drainage of fluid. No stoma Surgical Site Infection needs antibiotic therapy additionally and reoperation. Similarly results are also find by Vermulst et al.²⁴ in a study that all are manageable easily.

The biological process of wound healing consists of a series of complex interactions between cells, cytokines, and the extracellular matrix. Sometimes, the healing time is relatively long due to seroma formation.

The small orifice in the center of the wound allowed self drainage in the PSC group, so wound healing occurred more quickly due to less seroma formation. Murray et al.²⁵ compared the patients of CPC with the patients of open wound retrospectively and find no increase in incisional hernias, hospital stay, fistula formation in between these two groups like SSI rate 36% in CL group.

In these and also in our study the follow up length not properly exclude the increasing incidence of hernias incisional that is known as SSI late complication.

In a study, it was concluded that, SSI was 36.67% in primary closure and 10% in Purse-string closure group.¹³

In another study, it was reported that, Surgical Site Infection occurred in 15.7% and was more frequent in the Primary Closure group than in the Purse-string closure group 21.4% vs. 10%. Time of hospital stay in the Purse-string closure group was shorter than it was in the Primary Closure group (14.79 days vs. 16.44 days).¹⁴

In another study, it was found that, infection occurred in Purse-string closure patients 2.9% and in Primary Closure patients 21.8%. Time of hospital stay in the Purse-string closure group was shorter than it was in the Primary Closure group (6.55 days vs. 6.78 days).¹⁵

Conclusion

The frequency of surgical site infection and mean length of hospital stay after stoma reversal, purse-string suturing technique is significantly less than

Table 1: Stratification of Surgical Site Infection in Both Groups with Respect to Gender

Surgical site infection in males	Groups		Total	P-value
	Purse-String Closure	Conventional Primary Closure		
Yes	3	9	12	0.048
	7.3%	23.1%	15.0%	
No	38	30	68	0.594
	92.7%	76.9%	85.0%	
Surgical site infection in females				
Yes	1	2	3	0.594
	3.4%	6.5%	5.0%	
No	28	29	57	0.594
	96.6%	93.5%	95.0%	
	29	31	60	

Table 3: Stratification of Length of Hospital Stay in Both Groups with Respect to Age

Length of hospital stay	Age groups	Groups	n	Mean	Std. Deviation	p-value
	Conventional Primary Closure	28	7.32	1.25		
41-55 years	Purse-String Closure	20	5.75	1.33	0.000	
	Conventional Primary Closure	25	7.44	1.19		
>55 years	Purse-String Closure	32	5.75	1.02	0.000	
	Conventional Primary Closure	17	7.24	1.15		

conventional primary closure technique.

Conflict of Interest: None

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Table 1: Stratification of Surgical Site Infection in Both Groups with Respect to Gender

Age groups	Surgical site infection	Groups		Total	P-value
		Purse-String Closure	Conventional Primary Closure		
25-40 years	Yes	1	5	6	0.227
		5.6%	17.9%	13.0%	
	No	17	23	40	
		94.4%	82.1%	87.0%	
	Total	18	28	46	
		100.0%	100.0%	100.0%	
41-55 years	Yes	2	4	6	0.556
		10.0%	16.0%	13.3%	
	No	18	21	39	
		90.0%	84.0%	86.7%	
	Total	20	25	45	
		100.0%	100.0%	100.0%	
>55 years	Yes	1	2	3	0.230
		3.1%	11.8%	6.1%	
	No	31	15	46	
		96.9%	88.2%	93.9%	
	Total	32	17	49	
		100.0%	100.0%	100.0%	

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Authors Contribution

NS: Conceptionlization of Project

AA: Data Collection

KA: Literature Search

KWA: Drafting, Revision

AM: Writing of Manuscript

Association of Lifestyle Factors with Sub-optimal Health Status Among Undergraduate Medical Students: A Cross Sectional Study

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Abstract

Sub-optimal health status is a gray state of health interceding between health and disease, causing reduction in vitality and adaptability in absence of any diagnosed illness. It is considered as a precursor to disease state whose prevention will decrease burden on healthcare system.

Objectives: To assess the burden of suboptimal health status and analyze its association with lifestyle factors among undergraduate medical students.

Methods: A cross sectional study conducted at King Edward Medical University, Lahore, Pakistan. Questionnaires based upon "Sub-Health Measurement Scale V1.0 (SHMS V1.0)" and "Health Promoting Lifestyle Profile-II (HPLP-II)" were distributed among medical students of different years and 379 responses were completed. The data was entered in SPSS version 23 using quantitative variables. Chi-square test was employed to determine association of dependent with independent variables.

Results: Frequency of the Sub-optimal health status and Health among individuals of study population was found to be 78.1% (296) and 21.9% (83) respectively. A significant positive association of lifestyle factors with Sub optimal Health Status was found ($p < 0.005$). There was a slightly high frequency of SHS among females than males and day scholars than hostellers. The respondents having SHS had lower mean values for each HPLP-II dimension relative to those who were reported as healthy.

Conclusion: There is a high frequency of SHS among medical students. Poor lifestyle is a risk factor as a significant correlation exists. It can be prevented by adopting a healthy lifestyle.

Key Words: Sub optimal, SHS, Health, Lifestyle, Dimensions.

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Introduction

Sub optimal Health status (SHS) is recognized globally as a pressing public health issue. The term first coined by a Chinese scholar Wang,^{1,2} is defined by WHO as a grey state of health, intervening between health and disease³ which is characterized by decline in vitality, physiological function and the capacity for adaptation with no defined, diagnosed

underlying illness. Individuals with SHS frequently experience symptoms, such as fatigue, headaches, dizziness, depression, anxiety, systemic ailments (e.g., disorders of the digestive system, cardiovascular system, urinary system, etc.) and non-specific pains (e.g., back pain and chest pain).² As a result, SHS subjects often experience compromised quality of life and frequent hospital visits incurring costly medical treatment.^{2,4}

The concept, though relatively contemporary in Western biomedicine, is being widely accepted and under study in other countries such as Japan, Canada and Australia. In a survey in 1998, a group of researchers conducted an examination of 6000 asymptomatic "healthy people" which showed that 72.8% were in the suboptimal health status range.⁵ Despite having high prevalence, the causes of SHS remain obscure. According to a large body of literature, lifestyle beha-

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aviors are considered as one of the most crucial elements affecting health^{2,6,7} and poor lifestyle factors such as work-related and study-related stress, sedentary lifestyle, insufficient sleep and unhealthy eating habits may be associated with SHS.^{8,9,10,11} There is substantial empirical evidence which shows that practicing adverse health behaviors increases an individual's susceptibility to negative health outcomes. Conversely, chronic disease prevention through healthy lifestyle behaviors is an accepted approach resulting in health promotion.

Medical University education and training can be a challenging experience for students as they are exposed to various psychosocial stressors that may result in undesired changes in health and lifestyle habits.^{12,13,14} Despite well documented advantages of health promoting behaviors, several studies have shown that university students exhibit behaviors of unhealthy lifestyle, particularly insufficient physical activity and responsibility for health. Various studies have concentrated on assessment of knowledge and practices regarding nutrition, exercise, sleeping habits, smoking and alcohol among medical students. In a cross-sectional survey in United Arab Emirate, a large proportion of medical students were found to be either underweight or plump and most believed that their activity levels were inadequate, with soaring stress levels and diets lacking in essential nutrients.¹⁵ Studies additionally report lack of proper physical activity and predominance of unhealthy habits like smoking and alcohol among a sizeable proportion of medical students.¹⁶

A study conducted on 11,144 medical students in China to assess SHS, found a frequency of 55.9% due to curriculum load and anxiety concluding that a significant positive association exists between poor lifestyle and the risk of SHS.⁹ Another study conducted at Renmin University of China studied association of individual lifestyle dimensions separately with SHS and highlighted that students with good sleep, physical activity and proper nutrition had low frequency of SHS.⁴

The main objective of the present study is to investigate the burden of SHS among medical students in King Edward Medical University, Pakistan and also to analyze its association with lifestyle. This will be laying the ground work for more studies related to the topic.

Methods

The study design was cross sectional and was conducted at King Edward Medical University, Lahore from March 2018 to December 2018.

Taking confidence interval as 95%, margin of error as 4% with SHS frequency anticipated to be 55.9%, a sample size of 379 students was calculated.⁹

Study participants were included by utilizing simple random sampling technique. The list of enrolled MBBS students from all years was entered in SPSS v23.0 which subsequently acquired sampling frame by random selection. The undergraduate MBBS students from first to fifth year, aged between 18 to 24 years were selected while students with any diagnosed disease were excluded. Institutional review board of KEMU reviewed and approved the study. Helsinki Declaration 1964 along with its later amendments were taken into consideration by all researchers.

A standardized questionnaire comprising of two components i.e. Suboptimal Health Measurement Scale V1.0 (SHMS V1.0) and Health Promoting Lifestyle profile-II (HPLP-II) were distributed among participants. The validity and reliability of both instruments had been proven in previous studies.^{9,17,18}

Before collecting the data, written informed consent form was signed by each respondent. Each questionnaire was completed by one student within approximately 30 minutes. The data obtained through questionnaires was analyzed using SPSS v23.0. Categorical variables were reported as frequencies while continuous variables as mean. Chi-square test was employed to determine association of dependent with independent variables considering P value of <0.05 as significant.

SHS was operationally defined by the physiological, psychological and social dimensions which in turn forms the basis of SHMS V1.0; hence health status of individuals was evaluated through this multidimensional questionnaire. It comprised of 39 questions, 4 of which focused on health self-evaluation. The remainder 35 items were divided into physiological, psychological and social dimensions. Physiological dimension was evaluated on the factors such as physical condition, organ function, body movement function and vigour.⁹ The psychological dimension comprised of positive emotion, psychological symptoms and cognitive function while the social dimension was based upon the factors including social

adjustment, social resources and social support. Each dimension was represented by fourteen, twelve and nine questions respectively, divided among these factors.⁹

There were five response elements for each question with their respective scores of one to five i.e., never = 1, occasionally=2, sometimes=3, constantly=4 and always =5. The dimensional scores were graduated with respect to their corresponding factors' score which in turn were based upon summed up score of respective questions. SHS was evaluated by first calculating each dimensional score separately and finally adding them together to get a raw score for a respondent. It was then converted into percentile by using the underlying formula:

$$\text{Converted Dimension in Score} = \frac{\text{original raw score in dimension-theoretically lowest score in dimension}}{\text{theoretically highest score in dimension-theoretically lowest score in dimension}}$$

The converted scores ranged from one to hundred and were utilized to interpret health status. By taking P10 point of each dimension as the standard, the threshold score for physiological, psychological and social dimensions were found to be 41.07, 54.17 and 58.33 respectively. When converted score of any dimension was more than dividing line score for that dimension, it was considered as SHS. If participant had SHS in all three dimensions, only then he/she was considered to be in sub optimal health status.

The second part of questionnaire was designed by Walker et al¹⁹ for lifestyle status evaluation of participant. It consisted of 52 questions that were divided into six dimensions: health responsibility (9 questions), nutrition (9 questions), spiritual growth (9 questions), interpersonal relationship (9 questions), physical activity (8 questions), and stress management (8 questions). There were 4 options to each question and they were scored accordingly (never=1, sometimes=2, often=3 and routinely=4). Keeping in view the original recommendation, mean of all 52 responses was computed to acquire HPLP II score; hence, it was ranked between 52 and 208 scores. Then they were divided into 4 parts: poor lifestyle (52-90), moderate (91-129), good (130-168) and excellent (169-208). (9) Higher scores showed better lifestyle.

Results

Out of a total of 379 medical students, the results indicated that students who were healthy were 21.9%

(83), while those with Sub Optimal Health Status (SHS) were estimated to be 78.1% (296).

When stratified according to gender, more females 79.0% (199) were found to be in the Sub optimal Health Range as compared to males 76.4% (97)

Stratification based upon type of accommodation/residence highlighted that more hostellers 78.5% (194) than day-scholars 77.3% (102) were found to be in SHS. [Table 2]

Based upon lifestyle status, 379 (100%) students were divided among four groups i.e., 'poor', 'moderate', 'good' and 'excellent' with each group comprised of 17 (4.5%), 248 (65.4%), 112 (29.6%), and 2 (0.5%) students respectively.

A significant variation of lifestyle was reported between males and females at good level (31.3% females relative to 26% males) but the differences were insignificant at poor, moderate and excellent level.

While in case of day-scholar and hostellers there was a significant difference of lifestyle at good (26.3% hostellers compared to 35.6% day scholars) as well as at moderate level (68% hostellers compared to 60.6% day scholars) but no significant difference at poor and excellent level. [Table 1]

As elaborated in Table 2, a statistical significance of

Table 1: Variation in Lifestyle based on Gender and Place of Residence

		Lifestyle Groups				
			Poor	Moderate	Good	Excellent
Gender	Male	Count	7	86	33	1
		%	5.50%	67.70%	26.00%	0.80%
	Female	Count	10	162	79	1
		%	4.00%	64.30%	31.30%	0.40%
Total		Count	17	248	112	2
		%	4.50%	65.40%	29.60%	0.50%
Type of Accommodation	Hosteller	Count	12	168	65	2
		%	4.90%	68.00%	26.30%	0.80%
	Day Scholar	Count	5	80	47	0
		%	3.80%	60.60%	35.60%	0.00%
Total		Count	17	248	112	2
		%	4.50%	65.40%	29.60%	0.50%

SHS association with Lifestyle was found by chi-square test. (p value < 0.005)

The physiological, psychological and social dimensions of SHS were also analyzed and their relation to

the lifestyle was found to be statistically significant using chi square test ($p < 0.05$) as described in Table 3.

Discussion

The present study focused on assessment of sub-optimal health status in undergraduate medical

Table 2: Health Status *Lifestyle Group Crosstabulation

		Lifestyle Groups				Total
		Poor	Mode- rate	Good	Exce- llent	
Health Status	Healthy	8	62	13	0	83
	SHS	9	186	99	2	296
Total		17	248	112	2	379
Chi-Square Tests						
	Value	df ^b	Asymptotic Significance (2-sided)			
Pearson Chi-Square	15.183 ^a	3	0.002			
Likelihood Ratio	15.584	3	0.001			
Linear-by-Linear Association	14.599	1	0			
N of Valid Cases		379				
a: 3 cells (37.5%) have expected count less than 5. The minimum expected count is .44.						
b: degree of freedom						

students and how their lifestyle affects their health status. The frequency of SHS was found to be 78.1% (296) in the sample population which is higher than what has been documented so far in other popula-

Table 3: Sub-Health Measurement Scale V1.0 Scores by Health status

		Lifestyle Groups				Total
		Poor	Mode- rate	Good	Exce- llent	
Physiological Group	Healthy	3	21	8	0	32
	SHS	14	227	104	2	347
Total		17	248	112	2	379
Psychological Group	Healthy	4	28	7	0	39
	SHS	13	220	105	2	340
Total		17	248	112	2	379
Social Group	Healthy	4	26	1	0	31
	SHS	13	222	111	2	348
Total		17	248	112	2	379
Pearson Chi square test						
	Value	df ^b	Asymptomatic Significance (2-sided)			
Physiological Group	2.293 ^a	3	0.005			
Psychological Group	5.706 ^a	3	0.013			
Social Group	15.183 ^a	3	0.002			
a: 3 cells (37.5%) have expected count less than 5. The minimum expected count is 0.16						
b: degree of freedom						

tions. Unavailability of objective clinical diagnostic tools for SHS could be also a contributing factor. Though the study instruments were standardized and had been used ubiquitously in other settings apart from China, this was a pioneer study employing the instrument in Pakistan. The result is supported by the studies conducted in China by Jianlu et al in which a high frequency of 55.9% was found.⁹ In contrast another study conducted in eastern and western areas of China showed a low frequency of 21%.²⁰

This study results were in consonance with other studies where SHS was positively associated with poor lifestyles in students but among social, physiological and psychological groups, the former two were more strongly associated than the latter which is inconsistent with the results of the study conducted by Bi j et al.⁹ This is a novel emerging finding and requires further studies in our population.

This study emphasized the difference of lifestyle and SHS frequency based upon gender as well as type of accommodation among medical students concurrently which was lacking in previous studies as only one aspect of the above two factors was focused.^{9,10} According to Chenjin et al, on the basis of Electronic device usage, smoking, drinking and nutrition, the SHS frequency was more among males than females which is differing from our result as score among females was established higher than males.²¹ This difference might be due to low physical activities among females according to our society.²²

The results of our study are supported by Hou H et al. who explained the increased susceptibility of females towards depression, anxiety and other neuropsychiatric disturbance due to psychological and physiological differences causing higher SHS frequency among them relative to males.²⁰

In view of association of SHS with type of accommodation i.e., day scholars and hostellers, not enough data is present. A study performed in New Delhi assessed health status specifically based upon type of accommodation and concluded that hostellers have a poor health relative to day scholars due to poor lifestyle factors like inadequate nutrition, sleep deprivation and lack of parental care but a proper association with the Sub-optimal Health Status was not assessed. In addition to assessment of lifestyle in view of type of accommodation our study also highlights its association with suboptimal health status. Hostellers had a higher frequency of SHS due to poor lifestyle

factors like deprivation of proper nutrition and increased psychological stress.²³ In contrast a research conducted in Turkey found no significant difference in mean score of HPLP II with respect to place of residence.²⁴

The statistically remarkable relationship between SHS and lifestyle factors highlighted in this study shows that a modification of lifestyle shall result in improved health outcomes. Early diagnosis of SHS will help to prevent the diseased state of individuals and forestall the progression of chronic diseases like hypertension, diabetes and coronary artery disease.²⁵

The results indicate physical and psychosocial instability among medical students which can be improved based upon the principles of HPLP-II. This can be achieved at community level through primary prevention with proper awareness and education. Improvement of eating habits, interpersonal relationship, spiritual growth, physical activity and stress management will cause decline in frequency of Sub-optimal Health Status.

The simple random selection of sample strengthened the study as it provided equal chance of selection to all the individuals within the target population therefore reducing sampling bias.

This research serves as an introductory study on the concept of Sub optimal health in Pakistan which focused on a niche population i.e., the undergraduate medical students. Other population domains should be undertaken in future studies for better understanding and comparison. Moreover, due to insufficient data, this study does not undertake the development of a SHS measurement scale specifically dedicated towards the population of Pakistan so further studies are required which exclusively take part in formulating such scale.

Limitations

As the study design was cross-sectional it does not provide an evidence of temporal relationship between exposure and outcome. The self-reported questionnaires by respondents could have led to information bias.

Conclusion

There is a high burden of Sub Optimal Health Status among medical students of King Edward Medical University. Moreover, a statistically significant relationship exists between life style factors and Health status

of the study population. Poor lifestyle is a risk factor for developing Sub-optimal Health Status which can subsequently be prevented by adopting a healthy lifestyle.

Conflict of Interest: None

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Authors Contribution

RZ, TS: Conceptionlization of Project

NY,JZ,TM,KHAS : Data Collection

RZ,JZ,TM: Literature Search

TS,NY,TM: Statistical Analysis

RZ,TS: Drafting, Revision

RZ,TS,JZ: Writing of Manuscript

Knowledge and Attitude of Cancer Patients Towards COVID-19 Pandemic

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Abstract

Objectives: This study is done to determine knowledge and attitude of cancer patients towards COVID-19 pandemic.

Methods: The study was conducted at Oncology Department, Mayo Hospital Lahore during August-October 2020. A questionnaire was used to determine knowledge and attitude of cancer patients towards COVID-19 pandemic. Data was analyzed using Spss version.23. Descriptive variables like gender, marital status, residence and disease characteristics were reported as means and frequencies. Intergroup analysis was done using Chi square test with $p < 0.05$ taken as significant.

Results: Of 269 enrolled patients, majority had advanced/metastatic disease (82.4%) and were being treated on outdoor basis (71.6%). Almost all (99.6%) were aware of COVID, electronic/print media being commonest source of information (62.7%). Though having different views, 81.5% considered it a natural calamity. During first wave, 22.4% had delayed their investigations while 34.7% faced treatment interruptions with average duration of delay being 55 ± 27 days. Traveling difficulties due to lock down was common reason of delay (54.8%). During this period 62.4% either noted worsening of symptoms or new symptoms. Despite all chaos, 89.9% selected for treatment continuation if provided with a chance and appropriate facilities. Correlation of delay in therapy with high level of education ($p = 0.013$) and perception about COVID-19 a natural calamity ($p = 0.041$) was found to be statistically significant.

Conclusion: Patients' perspective is important and should be taken into account in special circumstances like COVID. It will help in future in making efficient management planning of disease during unusual situations.

Key Words: COVID-19, cancer patients, Knowledge

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Introduction

Corona virus infection, named COVID-19 by WHO, is caused by SARS-COV2, which is primarily a respiratory virus. It emerged as global health problem by end of 2019, starting in China when people presented with pneumonia like illness and were diagnosed as having Corona virus infection.¹ WHO declared.² It as pandemic due to its rapid spread across the globe.⁽²⁾ It resembles other pneumonia in its

symptomatology but have a rapid rate of transmission.³ Most common clinical features include dry cough, fever, lethargy, sore throat, runny nose, alteration in taste and smell sensation. Severity of disease varies widely from asymptomatic to seriously sick requiring invasive ventilation^{4,5} Pakistan became affected by this pandemic by end of February with rapid surge of cases seen in March. To handle such an influx of COVID-19 cases, government imposed smart lock in the country.⁶ This situation affected routine social life and exerted detrimental financial issues⁷ With emergence of COVID-19, increased cost, decreased monthly income, travelling difficulties and fear of getting Corona virus illness led to marked reduction in acquisition of health care facilities.⁸ As per available data, cancer patients have higher risk of catching COVID-19 infection attributing greatly to frequent hospital visits apart from other patient and disease factors.⁹

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Methods

Patients of various malignancies presenting to Department of Medical Oncology and Radiotherapy, KEMU/ Mayo hospital Lahore, were enrolled in study after taking informed consent. Data was collected via questionnaire. Various demographic factors like age, gender, diagnosis, stage was inquired. Questions were asked to know about their level of knowledge about COVID-19, and how they responded to this pandemic in terms of preventive measures, delays in cancer care, if any, and its possible consequences on life of cancer patients.

Collected data was entered and analyzed using statistical package for social sciences (SPSS) version 23. An initial frequency counts and percentages were obtained for all the data. Descriptive statistics were reported as mean, frequency and percentage. Intergroup comparisons were performed using Chi-Square test. All p values < 0.05 were reported as statistically significant.

Results

The study subjects ($n=269$) comprised 128(47.6%) males and 141 (52.4%) females with age range between 11-66years (mean 44 ± 14.40). Almost all the patients (99.6%) were aware of COVID-19 pandemic. 184 (68.7%) were found to be aware of symptoms correctly and 218(81.3%) perceived it as a different illness from common flu. A total of 216(80.6%) patients were found to be following precautionary measures as advised by authorities. When asked about risk of acquiring COVID illness by cancer patients, 196 (73.1%) responded an increased risk to cancer patients while 72(26.9%) said that cancer patients have risk equivalent to general population. During first wave, 22.4% had delayed their investigations while treatment interruptions were seen in 34.7% patients with average duration of delay being 55 ± 27 days and traveling difficulties due to lock down commonest reason of delay (54.8%). During this period 62.4% either noted worsening of symptoms or new symptoms. Despite this great threat, and increasing number of cases, only 27(10.1%) patients opted for discontinuation of their cancer therapy while 241(89.9%) decided to continue the therapy when given a choice. Correlation of delay in therapy with high level of education ($p=0.013$) and perception about COVID-19 a natural calamity ($p=0.041$) was found to be statistically significant.

Table 1: Demographic Data of Patients Included in the Study

Demographics	Count	% age
Total Number of Patient	n=269	100
Gender		
Male	128	47.58
Female	141	52.42
Marital Status		
Married	229	85.13
Unmarried/Single	40	14.87
Residence		
Rural	127	47.21
Urban	142	52.79
Disease Characteristics		
Diagnosis	Count	% age
Unknown	17	6.32
Hematological Malignancies	75	27.88
Non-Hematological Malignancies	178	66.17
Stage	Count	% age
Early Stage	16	5.95
Advanced or Metastatic	253	94.05
Patient Characteristics:		
Qualification	Count	% age
Unknown	32	11.89
Illiterate	96	35.68
$\leq 10^{\text{th}}$ grade	117	43.49
$>10^{\text{th}}$ grade	24	8.91
Mode of Transportation	Count	% age
Private Transport	16	5.95
Public Transport	253	94.05
Diagnosis	Count	% age
Unknown	17	6.32
Hematological Malignancies	75	27.88
Non-Hematological Malignancies	178	66.17
Stage of Disease	Count	% age
Early Stage	17	6.32
Advanced or Metastatic	252	93.68
Mode of Treatment	Count	% age
OPD Basis	193	71.75
As Indoor Patient	76	28.25
Average Number of rooms in house	3.25 \pm 1.36	
Average Number of family members	7.29 \pm 2.33	

Discussion

SARS -COV2 infection has affected people of > 150 countries of the world with patients presenting primarily with respiratory symptoms though varied presentation due to involvement of other body systems is not uncommon. Virus mediated tissue damage, endothelial injury, impaired immune function are common pathogenic mechanisms explaining vast spectrum of its clinical manifestations.^{10,11}

Table 2: Knowledge of Cancer Patients Towards COVID-19

	Number	%age
Source of Information:		
Electronic/print media	168	62.7
Social media	29	10.8
Relatives/friends	66	24.6
Health care worker	4	1.5
View about COVID -19		
Natural calamity	212	81.5
Plot by government	12	4.6
Man-made virus	17	6.5
It has no existence	16	6.2
Is it a threat to life?		
Major threat	123	45.9
Mild threat	86	32.1
No threat at all	20	7.5
Mode of transmission		
Via droplets	153	57.1
Air borne transmission	21	7.8
Person to person	68	25.4
Via contaminated food	12	4.5
COVID case in friends/relatives		
Yes	69	25.7
No	200	74.3
Death due to COVID in friends/family		
Yes	16	6
No	253	94.05

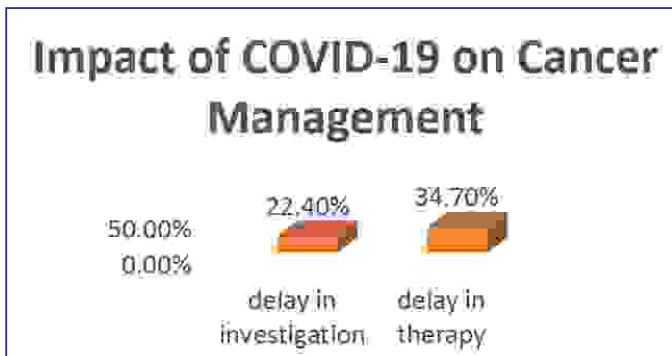


Fig. 1: Impact of COVID-19 on Cancer Management

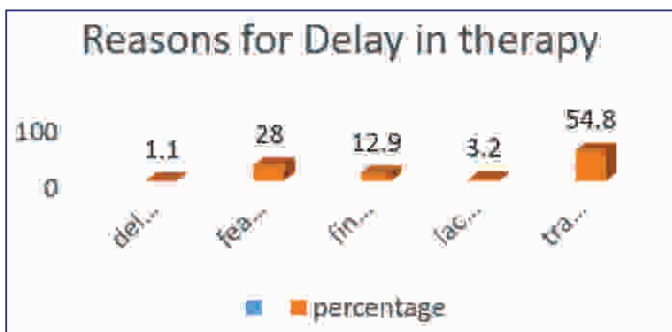


Fig. 2: Reasons for Delay in Therapy

Data has shown increased morbidity and mortality in cancer patients as compared with general population.

Old age at present-tation, weakened immune system, presence of multiple co-morbidities, need of frequent hospital visits are important reasons of increased vulnerability of cancer patients towards COVID-19 illness.⁹ In a study, all cause 30 days mortality was found to be significantly higher in cancer patients.¹² Diagnosis of cancer in general is considered as death sentence to affected. It is common observation that people when diagnosed with chronic lethal disease like cancer, let no stone unturned to get rid of it which often proves to be a futile effort. To achieve an effective cure/ symptomatic relief of symptoms is a physical and psychological trauma to patients and his/her caregivers. It poses social, psychological, financial burden on their lives but they continue their fight for survival.

COVID-19, with its strikingly high spread across the world, compelled governing authorities to impose lock down to control rate of transmission. It was implemented in almost all countries including Pakistan. This lock down apart from achieving its primary goal, exerted great difficulties in life of people especially developing countries like Pakistan where people suffered greatly not only from financial and social issues but also mental and physical health related issues. Health issues were partly from fear of getting corona infection and largely due to economic burden, travelling difficulties and non-availability of effective health care services.

In this study, we focused on perspective of cancer patients towards this pandemic. The study showed that advancement of telecommunication has led every one aware of the disease though majority of the respondents were illiterate and belonging to poor socio-economic status. Despite facing so many difficulties, majority having advanced incurable disease and different believes towards nature of COVID illness, treatment delays were seen in only 34.7% of patients which was largely due to travelling difficulties. It shows that although they have higher risk of potentially life-threatening illness, people opted for cancer treatment as they considered it more important likely because it is an issue which has greater impact on their health and lives. Important is to note that correlation of delay in therapy with level of education and their views about pandemic was found to be significant. It emphasizes that particular attention should be given to education of our people so they better understand exact nature of various illnesses

and their impacts which in turn lead to improvement in health of our people.

Conclusion

There is a strong need that we should focus on patients' perspective regarding their chronic debilitating illnesses like cancer in special circumstances like COVID-19 pandemic. This will help us in making effective strategies towards management of diseases like cancer without losing control during unexpected situations like pandemic.

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Authors Contribution

SY,MAK: Conceptionlization of Project

ZJ,NBB: Data Collection

SY: Literature Search

SY,AZ: Statistical Analysis

FRL: Drafting, Revision

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Trends of Self-Medication Amongst the Patients Visiting the Out-Patient Department of Combined Military Hospital, Lahore

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Abstract

Objective: The purpose of our study was to assess the trends of self-medication practices and to determine the prevalence, characteristics, related factors, and effects of self-medication among the patients conducted.

Methods: This descriptive cross-sectional study was on patients of Combined Military Hospital Lahore on a sample size of 365. The data was collected and entered in a predesigned questionnaire about self-medication later analyzed using SPSS version 17.0.

Results: The prevalence of self-medication was 95.3% and effectiveness was 87.7%. The common reasons for self-medication were prior knowledge of usefulness of remedy (63.3%), non-affordability of consultant charges (18.4%), and lack of time (21.9%). Frequently used medicines included antibiotics (30.1%), analgesics (69.6%), antipyretics (51.0%), and antihistamines (23.6%). Respondents claimed to receive information about these drugs from various sources including doctor (38.6%), previous prescription (31.8%), retailer seller (13.4%), family/friends (43.6%), media (7.9%) and other sources (1.6%).

Conclusion: It had been concluded that there is a high prevalence of self-medication. There is a need to raise public awareness about the appropriate use in order to prevent potential hazards of self-medication.

Key Words: trends, self-medication, out-patient department

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Introduction

Self-medication refers to intake of medicinal products to treat self-recognized symptoms or the intermittent or continued use of medication prescribed by doctor for chronic or recurring disease. It also involves self-administration of medication to family members especially children and the elderly.¹

Frequent use of medications like sedatives hypnotics like alprazolam could be addictive in contrast to analgesics or anti-pyretics. The access of over the

counter medications makes it easier for people to get drug of one's choice. The sale of certain drugs is although prohibited without proper prescription, but people used to get it via unfair means.

Formulations other than allopathic medications like herbal and hakeem medication has no check and unregulated in Pakistan so their consumption is vast. Certain medicines contain impurities and additives that can be injurious to human health.² These medications may also contain certain active harmful ingredients, like nonspecific beta blockers which can produce undesirable effects in certain individuals with disease like allergies, asthma etc. Self-medication involving inadequate and inappropriate dosage, incomplete treatment course and indiscriminate drug use may lead to evolution and rise of antimicrobial resistance.

The prevalence of self-medication ranges from 38.5% to 92% in various regions of the world.³ The local data is scanty, but it showed prevalence of around 51% to 84.4%. There is a paradigm shift towards self-medication with an increased number of

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people using medications on their own without proper consultation.^{4,5}

Keeping this in mind this study was designed with the sole purpose of finding the trend and prevalence as well the reasons behind the practice of self-medication amongst the population.

The present study was conducted with an intent to find the prevalence, cause of self-medication, different indications, the common factors compelling people to self-medicate and to assess the effectiveness and side-effects of self-medication.

Methods

This descriptive cross-sectional study conducted at Combined Military Hospital (CMH), Lahore on patients visited the outpatient department (OPD). A total of 365 individuals were recruited for the study via a convenience sampling method from various OPDs in CMH (medicine, surgery, ophthalmology, ENT, dermatology, dentistry, gynecology, pediatrics) irrespective of the underlying disorder that brought them to visit the hospital. A standardized questionnaire designed included demographic characteristics and questions related to self-medication after taking informed consent. The selected patients were verbally informed about the purpose of the study. They were assured about the confidentiality of their responses and personal information. The respondents were interviewed. The data was entered and analyzed by SPSS version 17.0. Descriptive statistics, including mean, standard deviation, frequency and percentage were used. Analytical statistics including chi square test was used to see the association of self-medication with other variables. P-value of <0.05 was considered statistically significant.

Results

Out of total sample size of 365, males were 202(55.3%) and females were 163(44.7%). The frequency of self-medication remained higher in illiterate than literate group shown in table#1. 348(95.3%) patients showed willingness for self-medication, while 17(4.7%) didn't use it very often. 320 (87.7%) patients responded in favor of the effectiveness of self-medication, while 45(12.3%) stated that it wasn't effective.

The most prevalent reason for self-medication was the existing knowledge of remedy (n=231, 63.3%),

followed by patients' lack of time (n=80, 21.9%) and high fees of doctor (n=67, 18.4%). Majority used allopathic medicine (n=305, 83.6%), while for homeopathic it was 12.6% (n=46) and Hakeem's medicine (n=46, 12.6%). Amongst the drugs used, the most common were analgesics (n=254, 69.6%), however antipyretics were 51.0% (n=186), antibiotics 30.1% (n=110) and antihistamines 23.6% (n=86).

Among the drug category, Allopathic medicine showed significant results (p = 0.001). The most significant reason of self-medication was found to be existing

Table 1: Various Demographic Characteristics

	Variable	Frequency(n)	Percentage(%)
Age Ranges	10-30	160	43.8
	31-50	150	41.1
	51-70	50	13.7
	>70	5	1.4
Gender	Male	202	55.3
	Female	163	44.7
Qualification	Illiterate	65	17.8
	School Level	135	37.0
	Undergraduate	111	30.4
	Graduate	36	9.9
	Postgraduate	18	4.9

knowledge of remedy (p=0.001), followed by not enough time (p=0.025), while high fees of doctor was less significant (p=0.045). There was high significance for fever (p=0.001), pain (p=0.001) and headache (p=0.001) while that for Allergy was a little less (p=0.014)

Among the drugs used, Analgesics and Antipyretics were most frequently used for self-medication. They showed the highest significance with p values of 0.001 each. They were followed by Antibiotics and Antihistamines with p values of 0.006 and 0.019 respectively. The most significant source of drug information were doctors (p=0.001) and family/friends (p=0.001), followed by previous prescription (p=0.004). The results showed that the number of participants who agreed with the high efficacy of self-medication were significant with a p value of 0.001. Similarly lack of experiencing any side-effects was also a highly significant response.

Among the most prevalent conditions for self-medication were headache (n=203, 55.6%), fever (n=195, 53.4%), pain (n=195, 53.4%) and allergy (n=93, 25.5%). Less prevalent conditions include heartburn (n=47, 12.9%), cough (n=37, 10.1%), diarrhea (n=26,

7.1%) and others (n=39, 10.7%).

Patients know which drug to use in self-medication mostly due to family/friends (n=159, 43.6%), doctors (n=141, 38.6%), and previous prescription (n=116, 31.8%). Less common sources were retailer seller (n=49, 13.4%), media (n=29, 7.9%) and others (n=6, 1.6%).

Most patients (n=216, 59.2%) didn't experience any side effects of self-medication, while those who did mostly complaint about nausea/vomiting (n=56, 15.3%), dizziness (n=3, 9.0%) and diarrhea (n=32, 8.8%). Less commonly experienced side-effects include allergic reaction (n=26, 7.1%), acidity (n=26, 7.1%), headache (n=18, 4.9%) and others (n=12, 3.3%).

Discussion

The trend of self-medication is variable ranging from 38.5% to 92% in various regions of the world.⁶ Local studies conducted in Pakistan showed prevalence of around 51% to 84.4%.

In the current study, allopathic medicine remained the mostly used category (n=305, 83.6%) in contrast with homeopathic and hakeem medications.

The most commonly ailment for self-medication was fever (n=195, 53.4 %) followed by generalized pain (n=195, 53.4%) and headache (n=203, 55.6%). Thus, the most frequently used drugs reported were analgesics (n=254, 69.6%) followed by antipyretics (n=186, 51%) and antibiotics (n=110, 30.1%). The results of our study are in consistent with previous studies which reflected the similar prevalence.⁷⁻⁹

63% of the participants reasoned that they already had knowledge regarding their remedy and the indications of the specific drug used, 21.9% of patients indicated lack of time. In addition, 18.4% of the participants were hindered to visit proper medical facilities due to the inability to afford the high fees charged by the doctors. These factors have been established by previous surveys as well.¹⁰

We also assessed the sources of information facilitating and encouraging the patients to self-medicate. It was found that the most pivotal role was played by family members and friends (n=159, 43.6%) in dispensing drug information. This was followed by referral to previous prescriptions (n=116, 31.8%). Interestingly the role of social media was found to be a contributing factor too (n=29, 7.9%).¹¹⁻¹⁶

Care must also be exercised to limit the development of antibiotic resistance as a result of increased tendency to self-medicate, an issue of a great concern now.²⁰ Studies conducted earlier signify that improper self-medication can lead to adverse drug reactions, increased morbidity, and mortality in addition to wastage of medical assets.¹⁷⁻²⁰

Our present study reflected that a significant percentage of participants (n=320, 87.7%) were agreed to the effectiveness of self-medication.

Limitations of this study are that this was a cross-sectional study where the sample was limited to patients visiting a single hospital located in an urban area, there is a need to collect evidence from rural area as well as the study does not accurately represent the trend across the country. Further as convenience sampling method was used and data collection was not blinded there is a chance of potential bias.

Conclusion

Self-medication was found to have an alarmingly high prevalence amongst the participants of this survey. However, keeping in mind the potential risks associated with self-medication, there is a need to spread awareness using means of social media, healthcare workers and health awareness campaigns. Efforts in the legislative policies are required to combat the outcome, primarily the disadvantages, caused by the increased trend to self-medicate by the availability of over the counter medicines and recommendations given by the ill-trained personnel at the pharmaceutical outlets. There is a need to educate people regarding potential hazards of outcomes.

Conflict of interest: None

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Authors Contribution

: Conceptionlization of Project
RAS : Data Collection
MF: Statistical Analysis
KAAB,PA,JS: Writing of Manuscript

Comparison of Berberine and Dexamethasone on Blood and Bronchial Inflammatory Cells of Ovalbumin Sensitized Guinea Pigs

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Abstract

Objective: To compare the anti-inflammatory effects of berberine and dexamethasone in ovalbumin sensitized guinea pigs.

Methods: This experimental controlled study was conducted in April, 2016 at Postgraduate Medical Institute, Lahore. Twenty- four healthy guinea pigs were selected for study. Six of these were assigned randomly in each group; normal control, ovalbumin (OVA) sensitized, berberine treated and dexamethasone treated groups. Airway inflammation was induced on day 0 and 14 by OVA injections via peritoneal route and by inhalation on 25th, 26th and 27th day in each group excluding the normal control. Berberine (1.8 mg/kg) and dexamethasone (20 mg/kg) were introduced via peritoneal route 30 minutes earlier to each trial in berberine treated and dexamethasone treated groups respectively.

Results: Total leukocyte count (TLC) in blood sample of berberine treated group ($9990 \pm 1346 \text{ mm}^3$) and dexamethasone treated group ($9054 \pm 1432 \text{ mm}^3$) was significantly low than OVA sensitized group ($14261 \pm 3151 \text{ mm}^3$). TLC of broncho-alveolar lavage (BAL) fluid in berberine treated group ($384 \pm 26 \text{ mm}^3$) and dexamethasone treated group ($306 \pm 86 \text{ mm}^3$) was significantly low than OVA sensitized group ($598 \pm 110 \text{ mm}^3$). Eosinophil percentage in blood of berberine treated (21.50 ± 3.08) and dexamethasone treated (13.33 ± 5.65) groups were significantly low than OVA sensitized group (30.33 ± 6.74), while eosinophil percentage in BAL fluid was 26.00 ± 6.69 and 21.00 ± 7.46 in berberine treated and dexamethasone treated groups respectively with significant difference from OVA sensitized group value of 40.00 ± 7.79 .

Conclusion: Berberine and dexamethasone both had reduced TLC and eosinophil percentage in both blood and BAL fluid as compared to OVA sensitized group but berberine is less effective than dexamethasone.

Keywords: berberine, dexamethasone, asthma, airway inflammation

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Introduction

Asthma is a common reversible chronic inflammatory condition of the lungs that leads to narrowing of the airways. Common symptoms

include breathlessness, wheezing, chest tightness and coughing. In 2016, it was estimated that 339.4 million people worldwide were affected by asthma.¹ In Pakistan, asthma is also prevailing very rapidly. Almost two million people are experiencing asthma per year and still 5% increase in cases is noted every year.²

The known risk factors for developing asthma include a combination of genetic predisposition and environmental exposure to various substances such as tobacco smoke and chemical irritants that may provoke allergic reactions or irritate the airways. Airways inflammation causes changes in the geometry and biomechanical properties with excessive production of mucus and consequent clogging and decreased lumen, resulting

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in development and persistence of airflow obstruction, predominantly in the early morning or evening periods.³ Multiple mechanisms are suggested for the production of this disease but the inflammation of smaller airways is the main feature. There is hyper-responsive of immune system to the innocuous stimuli. Asthma is exploited by multiple cellular elements and immune cells which include T lymphocytes, mast cells, macrophages, neutrophils, epithelial cells and eosinophils. Eosinophils play an important role in asthma pathogenesis, and eosinophilia is a typical hallmark of asthma in humans.⁴

Corticosteroids are considered to be the most potent and effective anti-inflammatory medications currently available for the symptomatic control and maintenance of atopic or non-atopic asthma, as recommended by GINA (global initiative for asthma) guidelines.⁵ Use of steroids is associated with a number of serious adverse effects. The loss of corticosteroid efficacy is an important issue in severe asthma management and may lead to poor asthma control and deterioration of airflow.⁶

Many people prefer to use different kinds of herbs for their treatment due to their folk knowledge and dislike conventional medicine because of their higher cost, adverse effects and reduced effectiveness.⁷ Impressively, recent studies have shown that berberine exerts anti-inflammatory and anticancer effects.⁸ In one study, berberine dose-dependently reversed the alterations induced by ovalbumin (OVA) in the asthmatic rats.⁹ There is scarce scientific research to evaluate the possible role of berberine in limiting the allergy induced inflammation in diseases like asthma. This study was planned with the objective to find out the possible anti-inflammatory role of berberine in asthma and its comparison with dexamethasone in OVA sensitized guinea pigs.

Methods

This is an experimental study which was conducted in April, 2016 at Pharmacology department of Post Graduate Medical Institute (PGMI), Lahore. Permission was obtained from research ethical committee for basic science of institute. Total twenty-four healthy guinea pigs of either gender weighing 340-500 gm were purchased from Lahore Zoo. (For one week, these animals were looked after at 22-24°C temperature for adaptation to the environment in PGMI. They were provided with plenty of water and food. The animals were checked for any sign of disease for exclusion from study.

After initial selection, they were assigned randomly to four groups by using lottery method. Airway inflammation was induced in animals of 3 groups excluding the normal control group as shown in table-1. The chemical used during study were ovalbumin (Sigma Aldrich, Poole U.K), alum (Biosector, Denmark), phosphate buffer saline (PBS) (Sigma Aldrich, Germany), berberine chloride (Sigma, USA), dexamethasone (OBS Pharma Pakistan) and chloroform (Scharlab S.L. European Union).

Blood sample was taken on 28th day of study by cardiac puncture while the animal was given light chloroform anesthesia.¹³ After blood sampling, guinea pigs were sacrificed with cervical dislocation. Bronchoalveolar lavage (BAL) fluid was collected by initially infusing and then withdrawing of 5 ml ice cold PBS through a cannula in the trachea and lungs.¹⁴

Total leukocyte count (TLC) was computed manually on Neubauer chamber both for blood and BAL fluid samples. Assessment of differential leucocyte count (DLC) was done with the help of Giemsa stained blood film under the oil immersion lens both for blood and BAL fluid samples.

Table 1: Allergic Airway Inflammation Induction and Drug Treatment

Groups	Sensitization on day 0 and 14	Intranasal challenge on day 25,26,27	Treatment on day 25,26,27
Normal control	1.5ml PBS by intraperitoneal route	PBS	Distilled water (DW) (5ml/kg) by intraperitoneal route half an hour before challenge
Ovalbumin sensitized	0.5ml OVA (100µg) + 1 ml alum (200mg) in PBS by intraperitoneal route ¹⁰	1% OVA in PBS	DW (5ml/kg) by intraperitoneal route half an hour before challenge
Berberine treated	0.5ml OVA (100µg) + 1 ml alum (200mg) in PBS by intraperitoneal route	1% OVA in PBS	Berberine (1.8mg/kg) ¹¹ by intraperitoneal route half an hour before challenge
Dexamethasone treated	0.5ml ovalbumin (100µg) + 1 ml alum(200mg) in PBS by intraperitoneal route	1% OVA in PBS	Dexamethasone (20 mg/kg) ¹² by intraperitoneal route half an hour before challenge

Data was entered and analyzed by using SPSS 20 software. After checking normal distribution, TLC and DLC were described as mean±standard deviation.

Table 2: Comparison of Blood and BAL Sample TLC (Mean±SD) in Study Groups (n=6)

Group=n=6	Blood	BAL
	Mean±SD (mm ³)	Mean ±SD (mm ³)
Normal control	8578.83±2065.65**	190.00±21.35**
Ovalbumin sensitized	14261.67±3151.36	598.66±110.94
Berberine treated	9990.33±1346.53*	#
Dexamethasone treated	9054.83±1432.29**	384.00±26.83**
ANOVA	<0.001	<0.001

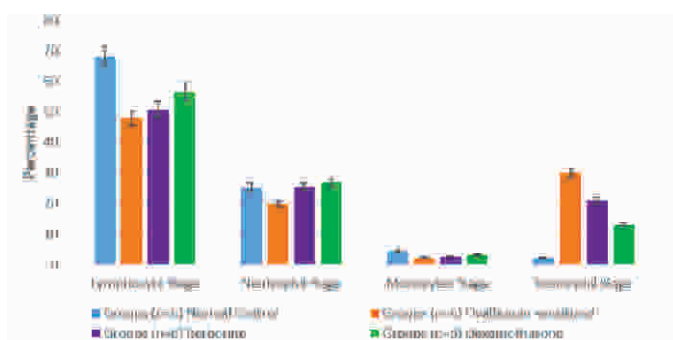
*p value ≤ 0.05, **p value ≤ 0.001 vs ovalbumin sensitized, #p value ≤ 0.001 vs normal

ANOVA was applied to compare TLC and eosinophil % of blood and BAL fluid. The group mean difference was detected by applying the post hoc Tukey's test. Statistically significant p-value was regarded as ≤ 0.05.

Results

The TLC in blood and BAL fluid samples of OVA sensitized group was markedly higher as compared to normal control. Berberine and dexamethasone treated animals had significant lower blood and BAL fluid TLC as compared to OVA sensitized group and insignificant higher than normal control (table-2)

Figure-1: Cluster Bar Chart Showing DLC in Blood



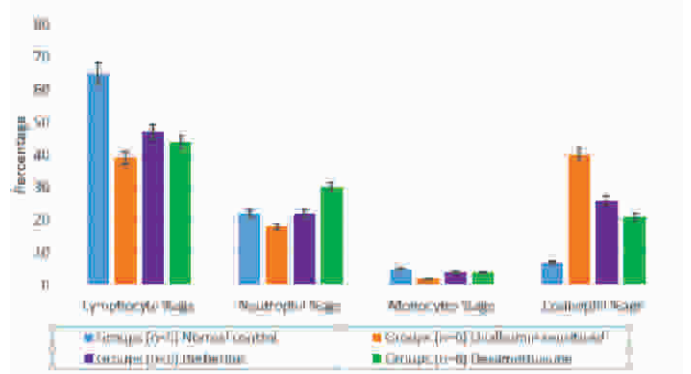
Sample of Study Groups

Figure-1 and figure-2 show DLC of blood and BAL fluid

Eosinophilic percentage in blood as well as BAL fluid was significantly higher in OVA sensitized group as compared to normal control. Berberine and dexamethasone treated animal had significantly lower eosinophilic percentage as compared to OVA sensitized control but higher as compared to normal control, with significantly less percentage in blood but not BAL fluid of dexamethasone group as

compared to berberine group (table-3).

Figure -2: Cluster Bar Chart Showing BAL Fluid



DLC in Study Groups

Discussion

Herbal plants have gained fame due to their cultural acceptance, lack of expense, minimum adverse effect and drug resistance.¹⁵ The berberine was selected in this study to find out its competency as an anti-inflammatory agent in the disease process of asthma in the guinea pigs which were sensitized with OVA. Then these results were compared with that of dexamethasone. The reason for selection of guinea pig as

Table 3: Comparison of Blood and BAL Sample Eosinophilic Percentage in Study Group

Group n=6	Blood Eosinophil %	BAL Eosinophil %
	Mean±SD (mm ³)	Mean ±SD (mm ³)
Normal Control	2.16±2.14**	7.5±4.9**
Ovalbumin Sensitized	30.33±6.74	40.00±7.79
Berberine	#	#
Dexamethasone	21.50±3.08*	26.00±6.69**
ANOVA	<0.001	<0.001

*p value ≤ 0.05, **p value ≤ 0.001 vs ovalbumin sensitized, #p value ≤ 0.001 vs normal, ° p value ≤ 0.05 vs dexamethasone

experimental animal was due to their similarities in the airways structure and disease process of asthma in human beings.

Our study demonstrates higher blood TLC in OVA sensitized group when compared with normal control group and difference was statistically significant with p-value 0.001. The results are complemented by the observations made by Arora et al (2016) in their study, of increased blood TLC levels in disease group as compared to the normal group.¹⁶

The decreased blood TLC levels were observed in berberine treated group as compared to OVA sensi-

zed group but these values were higher than normal control group. The similar effects were produced by berberine in a study conducted by Mahajan and Mehta, 2011.¹⁷ In our study, highly significant (p-value 0.001) lower levels of blood TLC were exhibited in dexamethasone treated group in comparison to OVA sensitized group. Arora et al (2016) and Murad and Hassnain (2014) have also revealed similar results after dexamethasone administration in murine model of asthma and OVA sensitized guinea pigs with p-values of 0.01 and 0.05 respectively when matched with sensitized groups.^{16,18} There is no study to compare the effect of berberine on blood TLC.

According to the results of current study, high count of white blood cell was noted in BAL after sensitization with OVA. The number of white blood cells was decreased more in both the treatment groups as compared to the group sensitized with OVA having a p-value of 0.001. In a rat model of asthma, orally administered berberine lowered BAL fluid TLC with p-value < 0.05.⁹ Difference in significance of results may be due to difference in route of administration and animal species.

Eosinophils play important role in asthma pathogenesis and this study demonstrates higher level of eosinophil percentage in blood and BAL samples of OVA sensitized group as compared to berberine treated group with a significant p-value of 0.05. Similar results were expressed in a study conducted by Mahajan and Mehta (2010) after treatment with β sitosterol compound from herb *Moringa oleifera*.¹⁷ The ratio of eosinophil in blood was significantly lesser (with p-value 0.001) in dexamethasone treated group when compared with ova sensitized group. These results are in accordance with the findings (with p-value 0.001) of Naik et al. (2013) study.¹⁹ The less significant levels (p-value 0.05) of TLC and eosinophil in BAL fluid were observed in similar asthma model with smaller doses of dexamethasone by Murad and Hassnain (2014).¹⁸

Overall impression of this study is that berberine and dexamethasone treatments have decreased the count of total leukocytes and eosinophils in blood as well as BAL fluid samples but berberine is less effective than dexamethasone.

This study is limited to evaluation of basic markers of allergic inflammation. Literature is available for possible role of berberine as suppressant of mast cell

degranulation²⁰ and inhibitor of cytokine production²¹ including interleukins²² which are involved in pathophysiology of asthma. Further studies on effect of berberine on airway hyperresponsiveness will confirm its role in prevention or treatment of allergic airways diseases.

Conclusion

Berberine is an effective anti-inflammatory agent in allergic asthma. These findings reveal the fruitful use of berberine to mitigate inflammatory process causing worsening of asthma.

Conflict of interest

None

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- CS:** Conceptionlization of Project
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Analgesia for the Change of Dressing in Burn Victims: A Comparison Between Oral Ketamine and Oral Dexmedetomidine

Faridah Sohail,¹ Lala Rukh Bangash,² Waqar Azim,³ Farah Arshad,⁴ Anum Anwar,⁵ Aaifa Khalid Niazi⁶

Abstract

Objective: To compare the efficacy of oral ketamine with oral dexmedetomidine for providing adequate analgesia for change of dressing in burn patients in burn dressing room.

Methods: This randomized controlled trial was carried out in Jinnah Burn and Reconstructive Surgery Center, Lahore, from April 2019 to September 2019 after getting the approval from the Ethical Committee of Jinnah Hospital / Allama Iqbal Medical College, Lahore. 80 patients between 20 to 50 years, with 1st and 2nd degree burns and 20 to 40% of total body surface area involved were allocated in two groups A and B. The patients in group A received oral ketamine at a dose of 5mg/kg in 15 ml of water 30 mins while those in group B received dexmedetomidine, 4 ug/kg orally, in 15 ml of water 30 mins before the start of dressing change. The change of dressing was carried out with continuous vital monitoring. Pain was assessed via visual analogue scale (VAS) and sedation via Ramsay sedation score. All the observations were recorded on the predesigned proforma. SPSS version 21 was used for data analysis.

Result: The baseline mean VAS score of patients in group A was 7.67 ± 0.55 and in group B was 7.70 ± 0.57 (p value = 0.799). Significant decrease in pain score in both groups was noted after 30 mins of drugs administration (p=0.000). Also a significant difference in pain scores was seen between the two groups (p< 0.05), with the patients in group A having lower pain scores as compared to patients in group B.

Conclusion: both ketamine and dexmedetomidine provide adequate analgesia for the change of burn dressing when administered orally with ketamine providing better analgesic state as compared to dexmedetomidine.

Key Words: Burn, ketamine, dexmedetomidine, analgesia.

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Introduction

Burns are one the leading causes of injuries inflicted to human body. The damage to the sensory nerve endings leads to considerable pain. The initiation of generalized inflammatory reaction further adds to the insult and compounds the morbidity and mortality.

In the present days frequent change of dressings is the hallmark of management of burn injuries. This, however, adds on the pain suffered by the burn victim. Apart from these acute pains, the burn victims develop neuropathic pain later on.^{1,2} In the modern era where various options for pain control are available, managing acute burn pain is still a challenging task. Inadequate pain control leads to various deleterious sequels including delayed wound healing, sleep disturbance, anxiety and post traumatic stress disorder.³

Ketamine, a phencyclidine derivative, has been well known for its analgesic properties. Apart from NMDA receptors, it acts on other receptors including opioid receptors to modulate pain. Ketamine is successfully used in various burn centers for management of acute pain. However, it comes at the cost of side effects like hallucination, agitation and emergence phenomenon.³⁻⁵

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Dexmedetomidine has emerged as a newer drug providing good sedation and analgesia but with little respiratory depression. However, hypotension and bradycardia are observed with its intravenous use.^{5,6}

Oral route of drug administration is a convenient one but studies on the oral use of dexmedetomidine are scarce. This study is thus designed to compare the efficacy of oral ketamine with oral dexmedetomidine for providing adequate analgesia for change of dressing in burn patients at burn dressing room.

Methods

This randomized controlled trial constituting of 80 patients was carried out in Jinnah Burn and Reconstructive Surgery Center, Lahore, from April 2019 to September 2019 after getting the approval from the Ethical Committee of Jinnah Hospital/ Allama Iqbal Medical College, Lahore.

The patients included in the study belonged of American Society of Anaesthesiologist (ASA) class I and II, both male and females having age between 20 to 50 years, with 1st and 2nd degree burns and 20 to 40% of total body surface area involved. Patients having diabetes mellitus, hypertension, ischemic heart disease, compromised renal or hepatic functions, any psychiatric illness or history of allergy to the drugs used in this study were excluded. Patients with electric burn were also not included in the study. Informed consent was taken from all the patients enrolled in this study.

All the patients included in the study were given tab. bromazepam 3mg orally at night time and injection morphine 0.05mg/kg intravenously before the start of change of dressing. Standard NPO protocols were followed. The patients were randomly allocated in two groups, A and B, with 40 patients in each group. The patients in group A received oral ketamine at a dose of 5mg/kg in 15 ml of water 30 mins before the start of dressing change while those in group B received dexmedetomidine, 4 ug/kg orally, in 15 ml of water 30 mins before the procedure. The change of dressing was carried out as per protocol of the burn unit. Continuous vital monitoring i.e. heart rate (HR), non invasive blood pressure (NIBP) and oxygen saturation (SpO₂) via pulse oximeter was carried out throughout the procedure. These haemodynamic parameters were recorded on a pre designed proforma including before the administration of drugs, 5 mins, 30 mins, 60 mins and 120 mins after the drugs administration. Pain was

assessed via visual analogue scale (VAS) and sedation via Ramsay sedation score. Any adverse events were also noted and treated accordingly. Any patient requiring rescue analgesia was also noted and treated by giving injection morphine intravenously titrating the dose but not exceeding more than 0.05mg/kg. All the observations were recorded on the predesigned proforma.

Statistical Analysis

The data was analysed using SPSS version 21. Systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate, oxygen saturation, VAS score and sedation were analysed over a period of time using repeated measure ANOVA, with Tukey's method employed as a test of significance. P value < 0.05 was taken as significant. Mean was calculated for quantitative variables like age and body surface area burnt and t-test was used as test of significance with p value < 0.05 taken as significant. For qualitative variables like gender, need for rescue analgesia and occurrence of side effects like salivation and delirium frequency, chi square test was used as a test of significance, p value < 0.05 was considered significant.

Table 1: Physical Characteristics and Base Line Parameters of Two Groups

Parameters	Group A	Group B	P value
Age (years)	35.08 + 10.01	34.08 + 9.27	0.899
Gender	Male= 21 Female = 19	Male = 20 Female = 20	0.823
BSA Burn (%age)	29.58+ 6.94	30.12+ 7.15	0.728
SBP (mmHg)	122.63+18.81	123.50+17.51	0.83
DBP (mmHg)	73.75+ 10.36	74.87+ 11.68	0.65
HR (bpm)	99.62+ 12.08	102.70+12.76	0.272
SpO ₂ (%age)	97.83+ 1.05	97.65+ 1.29	0.55
Sedation (Ramsay scale)	1	1	-
Pain Score (VAS cm)	7.67 + 0.55	7.70 + 0.57	0.799

Results

Both groups were comparable in terms of gender, age, percentage of total body surface area burnt, initial pain score, sedation score and haemodynamic parameters as shown in Table-1.

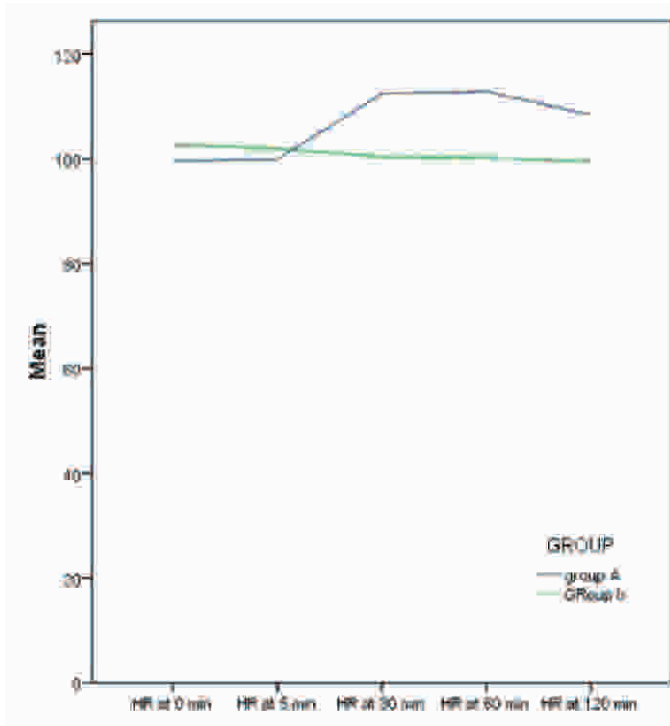
The baseline mean VAS score of patients in group A was 7.67 + 0.55 and in group B was 7.70 + 0.57 with p value of 0.799. Significant decrease in pain score in both groups was noted at 30 mins of drugs administration (p=0.000). Although patients in both groups

Table 2: Comparison of Sedation Score of Two Study Groups

	Group	Mean	Std. Deviation	N
sedation score at 0 min	Group A	1.00	.000	40
	Group B	1.00	.000	40
	Total	1.00	.000	80
sedation score at 5 min	Group A	1.00	.000	40
	Group B	1.00	.000	40
	Total	1.00	.000	80
sedation score at 30 min	Group A	2.00	.000	40
	Group B	2.00	.000	40
	Total	2.00	.000	80
sedation score at 60 min	Group A	2.75	.439	40
	Group B	2.00	.000	40
	Total	2.38	.487	80
sedation score at 120 min	Group A	2.92	.267	40
	Group B	2.00	.000	40
	Total	2.46	.502	80

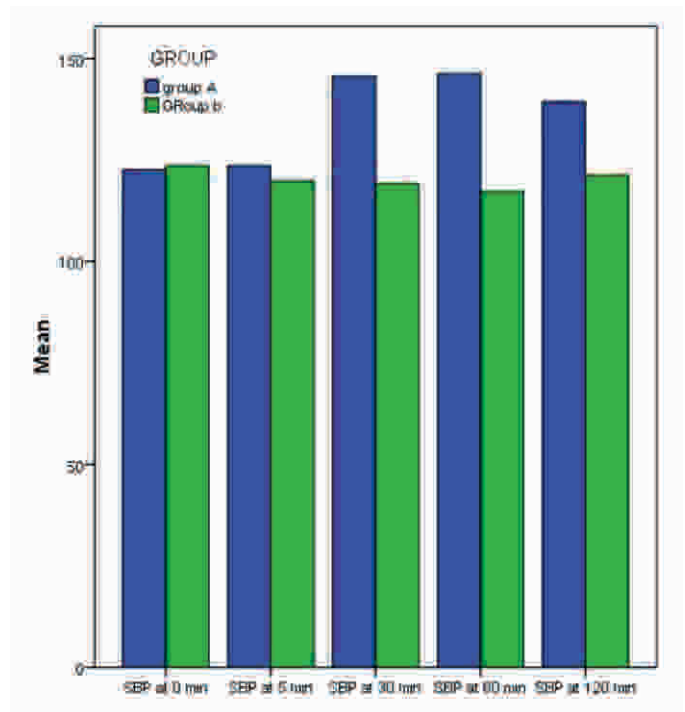
displayed significant pain relief, but a significant difference in pain scores was seen between the two groups as well ($p < 0.05$), with the patients in group A having lower pain scores and hence better analgesia as compared to patients in group B.

In both groups the baseline sedation score was 1 and at 30 mins it was 2. After 30 mins the sedation score in group A gradually increased whereas no change of score was seen in group B. (Table-2).

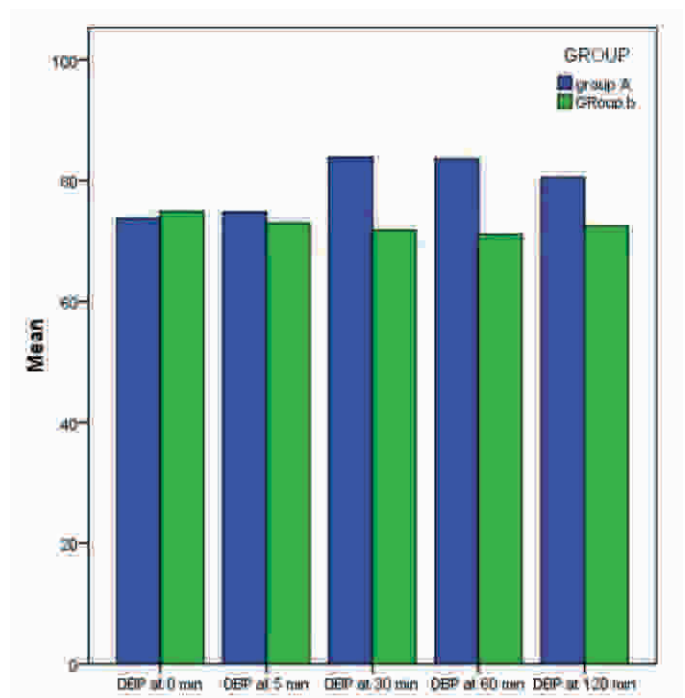


Graph-1: Comparison of Mean Heart Rate of Two Groups

Significant changes were noted in SBP, DBP and HR in both groups over time ($p < 0.05$). It was observed that the changes were significant between two groups as well, with these parameters showing a rising trend in group A while a decreasing trend in group B. (Graphs- 1,2,3,)



Graph-2: Comparison of Mean Systolic Blood Pressure of Two Groups



Graph-3: Comparison of Mean Diastolic Blood Pressure of Two Groups

Mean oxygen saturation at the time zero in group A was 97.83% + 1.05 and in group B was 97.65% + 1.29 with p value = 0.51. No significance difference in oxygen saturation was seen between the two groups at any point of time. No patient in any of the two groups had fall of oxygen saturation below 90% (Table-3).

7 out of 40 patients in group B (17.5%) needed rescue analgesia while none in group A needed it. In group A, 12 patients (30%) had delirium and 15 patients (37.5%)

Table 3: Oxygen Saturation of Two Groups Over Time

	Group	Mean	Std. Deviation	N	P value between groups
Saturation at 0 min	Group A	97.83	1.059	40	0.510
	Group B	97.65	1.292	40	
	Total	97.74	1.177	80	
Saturation at 5 min	Group A	98.00	.906	40	0.733
	Group B	97.92	1.047	40	
	Total	97.96	.974	80	
Saturation at 30 min	Group A	96.80	1.305	40	0.602
	Group B	96.95	1.260	40	
	Total	96.87	1.277	80	
Saturation at 60 min	Group A	96.97	1.209	40	0.712
	Group B	97.07	1.207	40	
	Total	97.02	1.201	80	
Saturation at 120 min	Group A	97.50	1.155	40	0.923
	Group B	97.52	1.154	40	
	Total	97.51	1.147	80	

had excessive salivation while there was no case of delirium or excessive salivation in group B.

Discussion

Burn injuries are considered one of the most debilitating of acute injuries. The degree of pain endured depends upon the thickness of burns and the area involved. It must be kept in mind that the full thickness burn in which even the sensory nerve endings carrying the nociceptive stimuli are damaged, are frequently surrounded by the areas of superficial burns which are much painful. Also different individuals have different threshold of pain. Hence the pain experienced by patients having similar burn injuries may also vary. Apart from the baseline pain suffered by the patients due to burn, the procedures carried out to accelerate the healing like frequent dressing changes, debridement and graftings further add to the acute pain suffered by the burn victims.¹⁻³

Ketamine is being used as an anaesthetic for over fifty

years now with the unique characteristic of producing dissociative anaesthesia. It is also an excellent analgesic agent even at subanaesthetic doses. It produces analgesia by acting as an antagonist at N-methyl-D-aspartate (NMDA) receptors. It not only blocks the channel by plugging the pore but also decreases the frequency of channel opening. However, NMDA antagonism is not the only mechanism which is responsible for the analgesic effects of ketamine.^{4,7} Various other mechanisms have been proposed which confers ketamine its analgesic property. These include Serotonin reuptake inhibition, partial agonistic effect at opioid receptors and interaction at GABA, cholinergic and dopaminergic receptors.^{4,7-9} Such is the quality of analgesia conferred by ketamine that it is now being used in emergency for the management of acute pain and also for chronic pain management¹⁰ including the opioid resistant pain.⁴ Due to its excellent analgesic profile, ketamine has been used for the change of burn dressings and graftings in burn victims for long time now.⁷ Recent studies have shown that ketamine also possess anti-depressant effect^{4,7,11}, a property which could be of additional benefit for the burn patients in whom the element of depression is not uncommon.¹² Ketamine can be given by various routes including intravenous which has 100% bioavailability, intramuscular with 93% bioavailability, oral, intranasal, rectal, subcutaneous, transdermal and epidural.^{4,7,13} The bioavailability of orally administered ketamine is low, around 16% to 25%. However much higher plasma levels of norketamine, a metabolite of ketamine, were seen when oral route is used for ketamine administration.^{4,5,11} Ketamine causes minimal respiratory depression. Upper airway reflexes are usually maintained.^{7,8} Some of the common side effects includes hallucination, delirium, excessive salivation, raised ICP, hypertension and tachycardia.^{4,7,9}

Dexmedetomidine is a relatively newer drug in the world of medicine. This highly selective centrally acting alpha-2 adrenergic agonist has sedative, amnesic, anxiolytic and analgesic properties. The sedation produced by dexmedetomidine is unique in the sense that it resembles natural sleep. Patients remain calm, lightly sedated and easily arousable.¹⁴⁻¹⁶ Apart from intravenous route of administration which has the highest bioavailability, this drug can be administered via intranasal, sublingual and oral route. However, the bioavailability after oral administration is low due to high first-pass metabolism.¹⁴ Dexmedetomidine

provides analgesia by acting on adrenergic receptors, thereby, having an opioid sparing effect. Due to the provision of stable haemodynamics, sedative, anxiolytic and analgesic properties, this drug is increasingly used for premedication and also in post operative period to provide analgesia. Despite shorter elimination half-life, the analgesic effect was observed to last for up to 24 hours.¹⁷ Dexmedetomidine is becoming popular for sedation in ICU for mechanically ventilated patients. Patients get more natural sleep, are less delirious, have better pain relief and are extubated earlier with shorter ICU stay.^{14,16} Common adverse effects associated with the use of dexmedetomidine includes a fall in blood pressure especially in frail patients and bradycardia. Patients may also experience heart blocks, dry mouth, pulmonary edema, lactic acidosis and paresthesia.¹⁴ However; these adverse effects are minimally seen with the oral use of dexmedetomidine.¹⁸

The results of our study show that both ketamine and dexmedetomidine provide effective analgesia for the dressing change in burn patients when administered orally. Analgesia provided by ketamine is significantly more as compared to dexmedetomidine. However, the patients receiving ketamine had experienced increase in the HR, BP, excessive salivation and delirium. These changes were not seen with the use of dexmedetomidine. Similar results were seen in the study conducted by Kundra et al.⁵ Ravipati et al used intra muscular dexmedetomidine as premedication for the dressing change and grafting in burn patients. Their results showed dexmedetomidine reduces the requirement of ketamine and propofol ($p < 0.0001$) and provides better haemodynamic state.¹⁹

Norambuena et al. concluded in their study that orally administered midazolam combined with ketamine provides better analgesia as compared to the combination of midazolam, codeine and acetaminophen for burn dressing and other related procedures in paediatric population.²⁰

Although dexmedetomidine has been used in infusion form for sedation and analgesia in burn victims in ICU but studies regarding its use as an analgesic for burn dressing change and that too in oral form are scarce.

Our study data shows that dexmedetomidine is orally effective for providing analgesia in burn patients. This route of administration will help to overcome the

problems of parenteral administration of this drug and improved patient compliance.

Conclusion

The study showed that both ketamine and dexmedetomidine provide adequate analgesia for the change of burn dressing when administered orally with ketamine providing better analgesic state as compared to dexmedetomidine. 17.5% patients who received dexmedetomidine needed rescue analgesia. However, side effects like excessive salivation and delirium seen with the use of ketamine (37.5% and 30% respectively) were not seen with the dexmedetomidine. Also dexmedetomidine provided better haemodynamic profile as compared to ketamine which causes tachycardia and hypertension; conditions detrimental for cardiac patients.

Conflict of Interest: None

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Authors Contribution

SF: Conceptionlization of Project

SF,RL,AF: Data Collection

RL,SF,AW: Literature Search

RL: Statistical Analysis

SF: Drafting, Revision

SF,RL: Writing of Manuscript

Recent Antimicrobial Susceptibility Patterns of Salmonella Isolates in A Tertiary Care Hospital Lahore

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Abstract

Objective: To determine the recent antimicrobial susceptibility patterns of salmonella isolates (typhi and paratyphi) in a tertiary care hospital of Lahore.

Methods: It is cross sectional retrospective study conducted out in King Edward Medical University(Pathology deptt)/Mayo Hospital Lahore. The study period is six months from May 2019 to October 2019(Peak months of Typhoid fever). During this six months study period, total of 4284 samples for blood culture were received that were inoculated on the macConkey and blood agar plates. The growths obtained were then processed through biochemical profiling and analytical profile index(API). The Kirby Bauer technique was used for antibiotic susceptibility testing and reporting was done on the basis of clinical laboratory standard institute(CLSI).

Results: During these six months, total 4284 blood samples were inoculated, out of which 433 growths were obtained. There were 84 strains of salmonella typhi isolated. Sensitivity pattern of different antibiotics showed that Azithromycin was sensitive to 70 (83.3%) isolates, imipenem in 72 (85.7%), ciprofloxacin to 56 (66.7%), gentamycin to 48 (57.1%), ceftriaxone to 45 (53.6%), cefepime to 20 (23.8%), chloramphenicol to 12 (14.3%) while ampicillin was least sensitive i.e. 8 (9.5%) isolates. There were 24 MDR(multidrug resistant) and 12 were XDR(extensive drug resistant) strains. We also found out that resistance to azithromycin drug is also emerging as 70 out of 84 strains were sensitive while remaining 14 were resistant.

Conclusion: According to recent antibiotic susceptibility against salmonella typhi, the most sensitive drugs are Carbapenems (imipenem or meropenem) these days. Second sensitive antibiotic is azithromycin.

Key Words: Antimicrobial susceptibility, Salmonella isolates, Carbapenems, Azithromycin.

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Introduction

Typhoid fever is an acute and sometimes life-threatening infectious disease. It remains an enormous public health threat in many developing countries (including Pakistan) due to inadequate access to safe water, poor sanitation system and inappropriate use of antimicrobial drugs.¹ An estimated 21 million

infections and above 1.6 lac deaths occur by typhoid fever worldwide each year. It is prevalent in Pakistan, that mostly affects children and teenagers.²

Salmonella typhi is responsible for almost 30% of community acquired bacterial bloodstream infections in Asian population, whilst salmonella paratyphi A is an emerging pathogen that causes upto 35% of all enteric fever episodes. Notably, paratyphoid fever has almost common features as that of typhoid fever.³

Salmonella enterica (typhi and paratyphi isolates) is a facultative intracellular and human restricted pathogen, predominantly transmitted by feco-oral route. Salmonella typhi is a gram negative, rod shaped, flagellated bacterium. It has a polysaccharide capsule that increases its virulence by inhibiting phagocytosis. It is H2S producing motile organism.⁴

Blood culture, urine and stool examination, serology

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and PCR (polymerase chain reaction) is available for diagnosing typhoid fever. Out of all these tests, blood culture and PCR is considered as gold standard.⁵

The WHO currently recommends imipenem, ampicillin, sulphamethoxazole-trimethoprim, flouroquinolones, 3rd generation cephalosporins (ceftriaxone, cefixime) and azithromycin(AZM) for the treatment of typhoid fever.⁶ Multiple drug resistant (MDR) typhoid fever is defined as resistance against three first line drugs including ampicillin, chloramphenicol and sulphamethoxazole-trimethoprim. In Pakistan it was reported to be 40%. After that flouroquinolones overtake as first line therapy but in early 2000, emerging resistance against flouroquinolones was increasingly being reported. In these circumstances, third generation cephalosporins become the treatment of choice for typhoid febrile illness in Pakistan.⁸

Currently sporadic cases of extensive drug resistant (XDR) typhoid are frequently being reported. XDR salmonella typhi is resistant to ampicillin, chloramphenicol, sulphamethoxazole-trimethoprim, flouroquinolones and ceftriaxone. For these cases, azithromycin and carbapenems are prescribed in XDR typhoid fevers. Recently it also has lost credibility due to emergence of resistance because of its overuse.^{7,9}

We planned to conduct this study in order emphasize the alternating trends of salmonella typhi antibiotic susceptibility to antibiotics in past few years in Pakistan, As XDR salmonella typhi infections is an alarming situation that is causing increase in mortalities.

Methods

It was a retrospective cross sectional study conducted at department of pathology, King Edward Medical University Lahore for six months i.e. May 2019 to October 2019. After ethical approval, 4284 samples of blood cultures received from the inpatient and outpatient departments of Mayo Hospital Lahore. All the blood cultures recieved were inoculated on two plates i.e blood and macConkey agar. The growth obtained was then further processed through biochemical profiling and analytical profile index (API) 20E. The Kirby Bauer technique was used for antibiotic susceptibility testing and reporting was done on the basis of Clinical Laboratory Standard Institute (CLSI) 2019.

Results:

Out of 4284 blood cultures , 433 had growths and the

remaining 3851 had no growths. There were 82 strains of salmonella typhi and 2 strains of salmonella paratyphi isolated from total 433 growths. The mean age of patients was 40.04±15.79 years. There were 56 (66.7%) patients of age 20-40 years, 18(21.4%) patients were of age 41-60 years and 10 (11.9%) patients were of age 61-80 years. There were 53 (63.1%) males and 31 (36.9%) females. Out of 84 cases, 82(97.6%) salmonella typhi while 2 (2.4%) had salmonella paratyphi. (Table 1)

In patients of age 20-40 years, salmonella typhi was present in 54 (96.4%) cases while salmonella paratyphi in 2 (3.6%) cases. In patients of age 41-60 years, salmonella typhi was present in 18 (100%) cases while salmonella paratyphi was not detected in this age group. In patients of age 61-80 years, salmonella typhi was present in 10 (100%) cases while salmonella paratyphi was not detected in this age group.

Sensitivity pattern of different antibiotics showed that Azithromycin was sensitive to 70 (83.3%) isolates, imipenem in 72 (85.7%), ciprofloxacin to 56 (66.7%),

Table 1: Demographics of Patients

n	84
Age (years)	40.04±15.79
20-40 years	56 (66.7%)
41-60 years	18 (21.4%)
61-80 years	10 (11.9%)
Gender	
Male	53 (63.1%)
Female	31 (36.9%)
Bacterium isolated	
Salmonella typhi	82 (97.6%)
Salmonella paratyphi	2 (2.4%)

gentamycin to 48 (57.1%), ceftriaxone to 45 (53.6%), cefepime to 20 (23.8%), chloramphenicol to 12 (14.3%) while ampicillin was least sensitive i.e. 8 (9.5%) isolates. (Table 2)

Out of these 84 strains, 24 (28.57%) were multidrug resistant (MDR) and 12 (14.28%) were extensive drug resistant (XDR) strains of salmonella typhi.

In this study we also found that resistance to azithromycin drug is also evolving. As out of 84 strains of salmonella typhi, 14 were resistant to azithromycin and remaining 70 were sensitive.

Discussion

The findings of this study clearly shows that MDR and XDR salmonella infections are emerging fastly. Most of the strains were sensitive to carbapenems and secondly to azithromycin. So, meropenem/imipenem and azithromycin are good choices of drug treatment for typhoid fever at present.

There was peak of MDR salmonella typhi epidemic in south and southeast Asia in the early 1990s. In these cases flouroquinolones were recommended. After

Table 1: Distribution of Sensitivity Pattern of Antibiotics in Salmonella Type

		Isolated bacterium		Total	p-value
		Salmonella typhi	Salmonella paratyphi		
Azithromycin	Sensitive	70 (85.4%)	0 (0.0%)	70 (83.3%)	0.001
	Resistant	12 (14.6%)	2 (100%)	14 (16.7%)	
Imepenem	Sensitive	72 (87.8%)	0 (0.0%)	72 (85.7%)	0.000
	Resistant	10 (12.2%)	2 (100%)	12 (14.3%)	
Ciprofloxacin	Sensitive	54 (65.9%)	2 (100%)	56 (66.7%)	0.311
	Resistant	28 (34.1%)	0 (0.0%)	28 (33.3%)	
Gentamycin	Sensitive	46 (56.1%)	2 (100%)	48 (57.1%)	0.215
	Resistant	36 (43.9%)	0 (0.0%)	36 (42.9%)	
Ceftriaxone	Sensitive	43 (52.4%)	2 (100%)	45 (53.6%)	0.183
	Resistant	39 (47.6%)	0 (0.0%)	39 (46.4%)	
Cefepime	Sensitive	18 (22.0%)	2 (100%)	20 (23.8%)	0.010
	Resistant	64 (78.0%)	0 (0.0%)	64 (76.2%)	
Chloramphenicol	Sensitive	10 (12.2%)	2 (100%)	12 (14.3%)	0.000
	Resistant	72 (87.8%)	0 (0.0%)	72 (85.7%)	
Ampicillin	Sensitive	8 (9.8%)	0 (0.0%)	8 (9.5%)	0.642
	Resistant	74 (90.2%)	2 (100%)	76 (90.5%)	

mutations of strains of salmonella typhi, flouroquinolones resistance developed that led to usage of parenteral ceftriaxone, that required hospitalization. Whereas antimicrobial resistance to these drugs is also increasing, such as recent emergence of XDR salmonella typhi organisms in Pakistan.⁷

The results obtained from blood cultures showed greater number of salmonella typhi isolates including extensive drug resistant strains that is a serious public health issue. Treatment of these extensive drug resistant salmonella infections is a big challenge for infectious diseases specialists. The only treatment options left are carbapenems and azithromycin antibiotics. Treatment plan of XDR typhoid includes intravenous meropenem (carbapenem) for one week followed by oral azithromycin.^{8,10} Carbapenems are very important as well as effective antibiotic treatment for typhoid fever but the presence of carbapenemase producing enterobacteriaceae is also a serious issue.^{9,11}

Small sample size, short duration study (6 months), antimicrobial pre-treatment and decreased sensitivity of blood cultures as compared to PCR are the main limitations of our study. Others include lack of minimum inhibitory concentration (MIC) and extended spectrum beta lactamases (ESBL) testing for different antibiotics.

Conclusion

It was concluded that carbapenems (meropenem or imipenem) and azithromycin are drugs of choice for XDR salmonella typhi infections now-a-days & antibiotic stewardship is required in order to prevent the prevailing resistance to different antibiotics.

In the background of rising MDR and XDR infections, healthy policy making, improved healthcare and institutional facilities and effective antibiotic stewardship is the need of hour to combat this problem.

Conflict of Interest: None

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Fetomaternal Outcome After Induction of Labor at Term in Patients with Gestational Diabetes

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Abstract

Objective: The objective of study is to determine the fetomaternal outcome after induction of labour at term in patients with gestational diabetes.

Methods: This study was conducted at department of Obstetrics and gynecology of Hameed Latif hospital, Lahore, Pakistan from March 2019 to October 2019. Seventy-nine pregnant women with gestational diabetes at term, undergoing induction of labour were included in the study after informed consent. Maternal outcome was studied by classifying different modes of delivery. Fetal outcome was measured on basis of APGAR scores and neonatal weight.

Results: There were 55/79 vaginal deliveries making vaginal delivery rate to be 66.9%. Mean birth weight of neonates was 3.15 + 0.558 kg. Mean APGAR Score at 1 min and 5 minutes were 7.7 + 0.6193 and 8.8 + 0.4793 respectively.

Conclusion: Labor induction in patients with gestational diabetes is associated with lower rate of cesarean delivery with a satisfactory fetal outcome.

Key Words: Gestational diabetes, induction of labour, maternal outcome, fetal outcome

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Introduction

Gestational diabetes mellitus is defined as a glucose tolerance disorder that manifests itself during pregnancy, is characterized by glucose levels that are above normal but below that diagnostic of diabetes and poses unique diabetes-related risks to both the mother and the unborn baby.¹

Gestational diabetes occurs in about 7-10% of pregnancies worldwide although the occurrence varies based upon its set criteria and the demographics of the population.² In Pakistan alone, a developing country, the prevalence of gestational diabetes was found to be between 3-4% as shown by research conducted in specific areas of the country.³ The prevalence of ges-

tational diabetes is directly proportional to the prevalence of type II Diabetes Mellitus in a population as well as the ethnic group, as research has shown that African, Hispanic, Indian, Pakistani and Asian women are more likely to develop gestational diabetes than Caucasian women of the same age.⁴ It's prevalence has seen to increase by nearly 30% in the past two decades especially in the developing countries as these countries are now being targeted by type II diabetes and its associated comorbidities. The increase in type II diabetes and its onset at a younger age can be well attributed to urbanization and sedentary lifestyles leading to significant obesity and insulin resistance in the populations.⁵

Gestational diabetes is associated with an increased risk of complications related to pregnancy and childbirth in both the mother and the baby. Gestational diabetes increases the risk of maternal complications like diabetic retinopathy, nephropathy and ketoacidosis and increases the likelihood of the mother developing full-blown type II diabetes mellitus later on in life.⁶ There are associated obstetric complications as well, including hypertensive disorders, cesarean deli-

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very, preterm birth, shoulder dystocia and slow labor.⁷ Perinatal complications include macrosomia, delayed intrauterine fetal development and respiratory distress.⁸ Gestational diabetes also causes neonatal complications like hypoglycemia, hypocalcemia, hyperbilirubinemia and polycythemia. One of its long term effects is the offspring being at risk for developing type II diabetes in early adulthood.⁹

Labor induction is a valuable and important obstetrical procedure. It is performed when prolongation of pregnancy is considered unsuitable for both maternal and fetal well-being.¹⁰ Mechanical methods of labor induction include the use of intracervical Foley's catheter and laminaria tents. Medical methods including oxytocin, prostaglandin and combinations of both. Cervical status and parity of the patient are two important factors that determine the outcome of labor induction.¹¹ Labor induction may lead to certain complications like failed induction, uterine hyper stimulation, fetal distress, abruptio placentae, uterine rupture, inadvertent preterm delivery, hyponatremia, hyperbilirubinemia, hypotonic uterus and postpartum hemorrhage. Hence it is important to assess the effects of induction on labor itself especially in patients with gestational diabetes to prevent added complications.

Timely detection and initiation of treatment is essential to prevent complications caused by gestational diabetes.⁸ Appropriate clinical management is that which is customized according to the patient's condition, is timed appropriately with no delay and carried out considering the woman's consent and informed decisions. This is vital especially in a country like Pakistan where the disease goes mostly unnoticed with no significant data regarding the prevalence of gestational diabetes and development of preventative strategies. Complication rates are higher in Pakistan due to poor glycemic control.⁹ This study was conducted at Hameed Latif Hospital, a tertiary care hospital in the metropolitan city of Lahore, Pakistan. It aims to assess the maternofetal outcomes in women with a history of gestational diabetes undergoing induction of labor to better understand the comorbidities associated with gestational diabetes at term and form a base for preventative and curative measures against it.

Methods

This cohort study was conducted at the Obstetrics and Gynecology department of Hameed Latif Hospital,

Lahore from March 2019 to October 2019. It was a prospective study which included both outdoor (OPD) and admitted pregnant patients. The patients were either attending antenatal OPD or medicine OPD or were admitted in the medicine or obstetric wards.

The inclusion criteria comprised known cases of gestational diabetes with no contraindications for vaginal delivery. The criteria for gestational diabetes was set as fasting sugar level of greater than 100 mg/dL and post-prandial sugar level of greater than 140 mg/dL during pregnancy. The exclusion criteria comprised known diabetics i.e. those with diabetes outside of pregnancy and those with history of previous uterine surgery.

Seventy-nine women pregnant patients with diagnosed gestational diabetes in whom labor was induced participated in the study. Labor was induced using tablets after measuring Bishop score and getting a score of 6. The women were between 15-40 years of age, primigravida as well as multigravida and their gestational age varied between 38-40 weeks.

Sampling technique used was non randomized purposive sampling. Informed consent was taken from the participants while keeping their identity anonymous and confidential. Information was collected after getting ethical approval for research from the participants via a detailed proforma. Proforma consisted of information regarding demographics, patient history, examination, investigations, labor induction, maternal and fetal outcome.

The results were analyzed using SPSS software version 23. The continuous variables were presented via frequency, mean and standard deviation. The categorical data was presented as frequency and percentages.

Results

Data was collected via proforma from 79 patients having gestational diabetes in whom labor was induced to study the maternofetal outcome. Majority of the patients (74.6%) were aged between 21 and 30 years. Mean age calculated was 25 ± 5.0252 . Most of the patients (58.2%, 46/79) were with their first pregnancy. Each patients' gestational age was also tabulated as 36 weeks onwards. 41.8% of the patients were at gestational age of 39 to 39+6 weeks, which makes about 33 patients out of 79 included in this group. Next most common gestational ages were 38-38+6 weeks (26.6%, 21/79) and 40 weeks or more (19%,

15/79) respectively. Gestational ages of 37-37+6 weeks (8.9%, 7/79) and 36-36+6 weeks (3.8%, 3/79) were less common than the rest. Mean gestational age was 39+1, with standard deviation calculated to be 1.0085.(Table 1)

Maternal outcome was assessed by grouping into spontaneous/operative vaginal delivery and lower segment cesarean section (LSCS). (Table 2). 55/79 (69.6%) patients had vaginal delivery out of which total 6 cases (7.6 %) of spontaneous vaginal delivery. Operative vaginal delivery was further classified into Ventouse and Forceps. Ventouse delivery comprised nearly half of the cases at 54.4%, with 43 cases out of 79. Forceps delivery had the same percentage as spontaneous vaginal delivery (7.6%) with total 6 cases only. Lower segment cesarean section was

Table 1: Sociodemographic Characteristics of Participants (n=79)

S/ No.	Sociodemographic Characteristics	No. of cases	Percentage	Mean	Standard Deviation
1.	Age in years				
a.	Up to 20	9	11.39		
b.	21-30	59	74.68	25	5.0252
c.	31 and above	11	13.92		
2.	Gravidity				
a.	Primigravida	46	58.23		
b.	Gravida 2	22	27.85	---	---
c.	Gravida 3	7	8.86		
d.	Gravida 4 or more	4	5.06		
3.	Gestational Age				
a.	36 – 36+6 weeks	3	3.79		
b.	37 – 37+6 weeks	7	8.86		
c.	38 – 38+6 weeks	21	26.58	39+1	1.0085
d.	39 – 39+6 weeks	33	41.77		
e.	40 weeks or more	15	18.99		

second to Ventouse only in terms of number of cases at 30.4% i.e. 24 cases out of the 79. The indications for LSCS were grouped into failed induction, fetal distress, both or failed progress of labor. (Table 3). The commonest indication was failed induction of labor with 14/24 cases (58.3%). Fetal distress was second in terms of occurrence, with 8/24 cases (33.3%).

Fetal outcome was assessed by neonatal weight in kilograms and Apgar score at 1 minute and 5 minutes after birth respectively. The greatest proportion of neonates weighed between 3.1 to 3.5 kilograms (39.2%, 31/79) followed by the range of 2.6 to 3.0 kilograms (31.6%, 25/79), 3.6 to 4.0 kilograms (20.3%, 16/79), 2.1 to 2.5 kilograms (5%, 4/79), 2 or less than 2 kilograms (2.5%, 2/79) and 4.1 kilograms and above (1.3%, 1/79), respectively. Thus, the results showed

that most of the neonates weighed between the range of 3.1-3.5 kg and 2.6-3.0 kg whereas the extremes of

Table 2: Maternal Outcome (n=79)

S/ No.	Maternal Outcome	No. of Cases	Percentage
1.	Spontaneous vaginal delivery	6	7.59
2.	Operative vaginal delivery		
a.	Ventouse	43	54.43
b.	Forceps	6	7.59
3.	Lower segment cesarean section	24	30.38

Table 3: Indication for Induction of Emergency LSCS (n=24)

S/ No.	Indication	No. of Cases	Percentage
1.	Failed induction of Labor	14	58.33
2.	Fetal distress	8	33.33
3.	Both above	1	4.17
4.	Failed progress	1	4.17

weight such as less than 2 kg and greater than 4 were kg demonstrated by very few (1-2) cases only. Mean weight was 3.15 ± 0.5582 kg.

Apgar score was calculated a 1 minute and 5 minutes of birth respectively. At 1 minute, 76% or around three quarters of neonates scored 8 with 60/79 cases. 15.2% of neonates had an Apgar score of 7(12/79), 7.6% had an Apgar score of 6 or less than 6 (6/79) and 1.3% of neonates had an Apgar score of 9 (1/79). None of the neonates scored 10 at 1 minute. Thus, the lowest score was 6 or less than 6 and the highest was 9. Compared to this, the lowest Apgar score at 5 minutes was 7 and the highest was 10. These two extreme scores were not demonstrated by many cases as only 2/79 neonates (2.5%) and 1/79 neonates (1.3%) scored 7 and 10 respectively. 81% of the neonates demonstrated a score of 9, with 64/79 such cases. Next to this, 15.2% neonates scored 8, with a total of 12/79 cases. Thus, the most common Apgar score was 8 at 1 minute and 9 at 5 minutes. Mean score at 1 minute was 7.7 ± 0.6193 . Mean score at 5 minutes was 8.8 ± 0.4793 .(Table 4)

Discussion

This study was carried out at a teaching hospital to reveal and analyze the maternal and fetal outcomes in women with gestational diabetes who underwent labor induction. 79 known cases of gestational diabetes were used for this study.

In this study, maximum patients (75%) were clustered

Table 4: Fetal Outcome (n=79)

S/ No.	Fetal Outcome	No. of Cases	Percentage	Mean	Standard Deviation
1.	Neonatal Weight/kg				
a.	2 or less than 2	2	2.53	3.15	0.5582
b.	2.1-2.5	4	5.06		
c.	2.6-3.0	25	31.64		
d.	3.1-3.5	31	39.24		
e.	3.6-4.0	16	20.25		
f.	4.1 and above	1	1.26		
2.	Apgar score				
a.	1 min				
	6 or less than 6	6	7.59	7.7	0.6193
	7	12	15.19		
	8	60	75.95		
	9	1	1.26		
	10	0	0		
b.	5 min				
	6 or less than 6	0	0	8.8	0.4793
	7	2	2.53		
	8	12	15.19		
	9	64	81.01		
	10	1	1.26		

in the age group of 21-30 years. This is in contrast with a study conducted in Jammu that unveiled an association between increasing age and gestational diabetes, thus inferring that women with normal glucose tolerance tests tend to be younger and those with gestational diabetes, older.¹² More than half of the patients (58.2%) were primigravida while the rest of the patients (41.8%) were multigravida. Although in a study advanced age, high BMI and family history of diabetes were seen as important risk factors for gestational diabetes, no significant correlation existed between gestational diabetes and parity, frequency and number of pregnancies and number of live births.¹³

Maternal outcome was studied by classifying different modes of delivery. The study showed that around 30 percent of the patients under study underwent Lower Segment Cesarean Section, making it the second most common mode of birth or maternal outcome. The most common maternal outcome was birth via operative vaginal delivery, with Ventouse method being 54.4 percent of the outcome and forceps delivery 7.6 percent of the outcome. A study conducted to assess the effects of a policy of labor induction at or beyond term compared with a policy of awaiting spontaneous labor on pregnancy outcomes on mother and children using randomized control trials (RCT) concluded that labor induction is associated with fewer perinatal deaths and cesarean sections but more operative vaginal births, the latter reinforcing the

results of our study.¹⁴ Observational studies carried out to assess maternal and fetal outcome following induction of labor showed that women with elective induction of labor had a higher odd of cesarean delivery compared to women with spontaneous labor.¹⁵ Two studies showed considerable differences in the outcome of cesarean delivery between women who had elective induction and those who underwent expectant management. In both the studies the percentages of cesarean section following induction were less than that concluded by our study i.e. 30 percent.^{16,17} Another study conducted in Southern India revealed that 32 percent of women with gestational diabetes under study had undergone cesarean deliveries.⁽¹⁸⁾ Higher risk for cesarean section have been reported from other studies.^{19,20}

Fetal outcome was assessed in terms of neonatal birth weight and Apgar scores at 1 minute and 5 minutes after birth. Most neonates in our study weighed between 3.1-3.5 kg (39.2%), followed by 2.6-3.0 kg (31.6%) and 3.6-4.0 kg (21.3%). Macrosomia is one of the adverse neonatal outcomes of gestational diabetes. Some studies report that 15-45% of newborns of women with gestational diabetes have macrosomia.^{21,22} The mean weight calculated in our study was 3.15 kg. The reason may be meticulous control of blood sugar levels which correlates to macrosomia. Mean gestational age at delivery in our patients was 39±1 weeks of gestation. Gestational age at induction is important in determining outcome in terms of weight of baby. Studies regarding induction of labor at 38 to 39 weeks of gestation have shown a decrease while those at or beyond 40 weeks of gestation show increased chances of macrosomia.^{21,22,23}

Mean scores at 1 min and 5 mins were 7.7 and 8.8 respectively in our study. A study aimed at finding an association between gestational diabetes and Apgar scores of full-term neonates, with mean Apgar scores at 1 min and 5 min of 7.8 and 8.9 respectively, concluded that maternal history of gestational diabetes does not appear to be associated with the 1-minute and 5-minute Apgar scores of full-term newborns of mothers with gestational diabetes as compared to newborns of mothers without a history of impaired glucose tolerance.²⁴ When compared to babies born to mothers without gestational diabetes, those born to mothers with it were at higher risk of having a lower five-minute APGAR score. In our study only 7.6 percent of newborns had low APGAR score at 1 minute and

none had low APGAR score at 5 minutes. In a study regarding neonatal outcomes according to different therapies for gestational diabetes, 5.6 percent had low Apgar score at the first minute and 1.1 percent had low Apgar score at the fifth minute. Thus, this study concluded that there was no risk of low Apgar at either first or fifth minute in newborns of women with gestational diabetes.²⁵

Our study had its limitations like only one parameter i.e. mode of delivery was used to assess maternal outcome whereas other parameters like maternal weight, body-max index and presence of preeclampsia and eclampsia were not studied. It is cross sectional study, a comparative study of induction of labour with nondiabetic patients should be planned. The association between maternal outcome and gestational age also requires more attention to know exactly the incidence rates of cesarean (or other modes of deliveries) at specific gestational ages.

Conclusion

The incidence of cesarean delivery in women with gestational diabetes who have undergone induction of labor is low in our study along with satisfactory fetal outcome in terms of birth weight and APGAR score. Proper selection of patients, adequate diabetic control and induction at 39 weeks leads to successful outcome.

Conflict of Interest: None

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Authors Contribution

NF: Conceptionlization of Project

AL: Data Collection

IS,KF: Literature Search

IS: Statistical Analysis

AA: Drafting, Revision

IS,GT: Writing of Manuscript

Anti-Oxidative Effect of Aqueous Garlic Extract (AGE) on Androgen Induced Changes in Ovaries of Prepubertal Female Rats

Yasmeen Bashir,¹ Nabeela Habib,² Samar Ashraf³

Abstract

Objectives: It has been documented that the administration of exogenous androgens to immature female rats produces polycystic ovaries. There is a substantial reduction of antioxidants in this condition, with an elevated risk of oxidative stress. The current research is intended to evaluate these effects and to assess the protection provided by aqueous garlic extract (AGE).

Methods: An experimental study conducted at University of Health Sciences, Lahore. The data was collected over a period of one month. Fifty female prepubertal rats, 21 days of age, were divided into five groups, A, B, C, D and E. Group A served as control. Group B received testosterone propionate (TP) subcutaneous for 14 days and served as disease control. Group C received testosterone propionate (TP) subcutaneous for 14 days and concomitantly Aqueous garlic extract (AGE). Group D receive testosterone propionate (TP) subcutaneous for 14 days and Aqueous garlic extract (AGE) from day 14-21. Group E received testosterone propionate (TP) subcutaneous for 14 days with no intervention till day 21. Blood samples of 50 female rats were drawn by doing cardiac puncture and clear serum was collected by centrifugation. This serum was used to assess the Catalase enzyme by using specific commercial kits.

Results: The concentration and activity of catalase enzyme in the female rats with polycystic ovaries showed significant decrease as compare to the healthy controls. The involvement of antioxidants to manage the polycystic ovaries may be helpful as secondary therapy to prevent oxidative damage.

Conclusion: The results showed that AGE with its antioxidative properties not only prevents the damage caused by oxidative stress, it also increased the level of serum catalase that helps to create a balance between beneficial oxidant generation and damaging oxidative stress.

Key words: Androgens, immature female rats, ovaries, antioxidants, oxidative stress, aqueous garlic extract (AGE), Catalase.

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Introduction

Recent research in human and non human primates suggest that elevated androgens play a significant role in the development of conditions resembling polycystic ovarian syndrome (PCOS).¹

Early exposure of androgens in young females, either due to environmental or genetic factors can cause polycystic ovarian syndrome (PCOS).²

Rodent models of polycystic ovaries have shown many characteristics similar to that in the human polycystic ovarian syndrome (PCOS) which includes hyperandrogenism, disrupted cyclicality, presence of follicular cysts/polycystic ovaries.³ Different androgens were used to develop polycystic ovaries in rodents like Dihydrotestosterone (DHT), estradiol-valerate, dehydroepiandrosterone (DHEA), and testosterone.⁴ In this study we used Testosterone propionate (TP) to develop a rodent model of the condition.

Oxidative stress (OS) has been found to play a signi-

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ficant role in the pathophysiology of Polycystic Ovarian Syndrome (PCOS).⁵ The imbalance between oxidants and antioxidants is commonly referred as oxidative stress. When the imbalance favors the oxidants, generation of excessive amounts of reactive oxygen species harm our body in various ways.⁵ Oxidants, which exist in two categories: reactive oxygen species (ROS) and reactive nitrogen species (RNS), are exposed to biological systems living in aerobic environments. Chemical species that are formed upon incomplete reduction of oxygen include superoxide anion (O₂⁻), hydrogen peroxide (H₂O₂), and hydroxyl radical (OH)⁶. Under normal conditions, scavenging molecules commonly known as antioxidants prevent overproduction of reactive oxygen species (ROS) by converting it to H₂O. There are two types of antioxidants in the human body: enzymatic and non-enzymatic antioxidants.⁷ Enzymatic antioxidants or natural antioxidants neutralize excessive reactive oxygen species (ROS) and prevent it from destroying the cellular structure. Enzymatic antioxidants collectively constitute catalase, superoxide dismutase and glutathione peroxidase. Non-enzymatic or synthetic antioxidants include vitamins and minerals which neutralize reactive oxygen species (ROS) directly, such as vitamin C, vitamin E, zinc, taurine and beta carotene.⁸

Allium Sativum (Garlic) is one of the herbs used in the everyday life of Asian countries, whether in raw or cooked form. Raw garlic homogenate is the main preparation of garlic used in various scientific studies, since it is the usual way of garlic consumption. Garlic

is known to contain natural antioxidants that can remove reactive oxygen species (ROS).⁹ Garlic has been shown to have several medicinal properties, including antioxidative, antithrombolytic,¹⁰ cancer preventive,¹¹ and cardio-protective effect.¹² The antioxidant effect of garlic extract by scavenging reactive oxygen species increases the levels of cellular antioxidant enzymes; superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (Gper) in the cells.¹³

Raw garlic homogenate has been documented to increase the development of endogenous antioxidants and minimize lipid peroxidation in the liver, kidney and heart of rats in a dose-dependent manner.¹⁴ It is very helpful in treating many conditions related to the male reproductive system. Therefore, the purpose of this research is to evaluate the antioxidative effect of aqueous garlic extract on Testosterone propionate (TP) induced changes in ovaries of prepubertal female rats.

Methods

An experimental study conducted at University of Health Sciences, Lahore. The data was collected over a period of one month. 50 female prepubertal albino rats, 21 days of age and 40-50gms in weight, were obtained from colonies raised at the Animal House, University of Health Sciences, held at a controlled temperature of 25^o± 2^oC, humidity 55 ± 5 and light and dark cycles of 12 hours each. The animals were fed on standard rat diet and tap water ad libitum. The experiment was carried out in accordance with the

Table 1: Showing Intervention and Dosage Schedule

GROUPS N=10	INTERVENTION/ TREATMENT	ROUTE OF ADMINISTRATION	DURATION	SACRIFICED
GROUP A	Propylene glycol 5ml/kg	Subcutaneous	Day 1 to 14	On day 15 th of experiment
GROUP B	Testosterone propionate 10mg/kg dissolved in 5ml/kg propylene glycol	Subcutaneous	Day 1 to 14	On day 15 th of experiment
GROUP C	Testosterone propionate 10mg/kg dissolved in 5ml/kg propylene glycol	Subcutaneous	Day 1 to 14	On day 15 th of experiment
GROUP D	Aqueous garlic extract 200mg/kg	Oral	Day 1 to 14	
GROUP D	Testosterone propionate 10mg/kg dissolved in 5ml/kg propylene glycol	Subcutaneous	Day 1 to 14	On day 22 nd of experiment
GROUP D	Aqueous garlic extract 200mg/kg	Oral	Day 14 to 21	
GROUP E	Testosterone propionate 10mg/kg dissolved in 5ml/kg propylene glycol	Subcutaneous	Day 1 to 14 (Animals were sacrificed a week later on day 21)	On day 22 nd of experiment

instructions and guidelines of Ethical Committee of UHS. The animals were randomly allocated to five groups, A, B, C, D and E using balloting method containing 10 animals each. Intervention and dosage schedule is given in table 1.

Method for Blood Collection

On day 15 of the study, animals of group A, B, and C were weighed and transferred to a bell jar one by one covered with a lid, containing a cotton swab soaked in chloroform. The animals were kept till they were completely under but still breathing; these were then placed on the dissection board in supine position. 5ml of blood was drawn by doing cardiac puncture with the help of 5cc disposable syringe; blood was then transferred to vacutainer and allowed it to stand for one hour, and then put these vacutainers in the centrifuge machine (EBA-20 Heittich) to centrifuge at a speed of 3000 revolutions per minute. Clear serum was then transferred by a micropipette in to sterilized eppendorf; these tubes were properly labeled before placing them in to the refrigerator set at -20°C. These blood samples were used to assess the serum Catalase enzyme by using specific commercial kits. Animals from group D and E were sacrificed on day 21.

Chemical

Testosterone propionate was purchased from Ipca Laboratories Ltd., Batch No.4002 TH1RN, India. The dose and method of preparation of aqueous garlic extract was adopted from the earlier work.¹⁵ Similarly the dose of TP was derived from the work reported earlier.⁴ Doses were adjusted according to the weight of the animals.

Statistical Analysis

The data was entered and analyzed by using SPSS 20.0. Mean ±SD were given for the quantitative variables. One way ANOVA was applied to compare means of variables among the control and experimental groups. Post hoc Tuckey’s test was applied to compare the means of groups. Chi-square test was

applied to categorical variables. P-value ≤ 0.05 is considered statistically significant.

Result

One way ANOVA test showing the difference was statistically significant when mean value of serum catalase (p-value <0.001*) of groups A, B, C, D and E were compared with each other. (Table 2. Fig.1). The post hoc Tukey’s test was applied to analyze the comparison of mean value of serum catalase among various groups. (Table 3. Fig.1). There is significant increase in the level of serum catalase in experimental group D. The disease control group had markedly lower levels of the enzyme, whereas experimental groups had significant higher levels of the serum catalase as compared to other groups.

Table 3: Shows Multiple Comparison of Mean Value of Serum Catalase Among Various Groups

(I) group	(J) group	Mean Difference (I-J)	Std. Error	p-value**
A	B	.0152	.0371	0.994
	C	.0101	.0371	0.999
	D	-.1539	.0371	<0.001*
	E	-.2111	.0371	<0.001*
B	A	-.0152	.0371	0.994
	C	-.0051	.0371	1.000
	D	-.1691	.0371	<0.001*
	E	-.2262	.0371	<0.001*
C	A	-.0101	.0371	0.999
	B	.0051	.0371	1.000
	D	-.1640	.0371	<0.001*
	E	-.2212	.0371	<0.001*
D	A	.1539	.0371	<0.001*
	B	.1691	.0371	<0.001*
	C	.1640	.0371	<0.001*
	E	-.0572	.0371	0.542
E	A	.2111	.0371	<0.001*
	B	.2262	.0371	<0.001*
	C	.2212	.0371	<0.001*
	D	.0572	.0371	0.542

*p≤0.05 is considered statistically significant. **Tukey HSD Test.

Table 2: Comparison of Mean Value of Serum Catalase Among Various Groups

Serum catalase	Group A	Group B	Group C	Group D	Group E	p-value
	Mean ±SD	Mean ±SD	Mean ±SD	Mean ±SD	Mean ±SD	
	0.101±0.084	0.086±0.083	0.091±0.111	0.235±0.066	0.150±0.047	<0.001

*p≤0.05 is considered statistically significant.

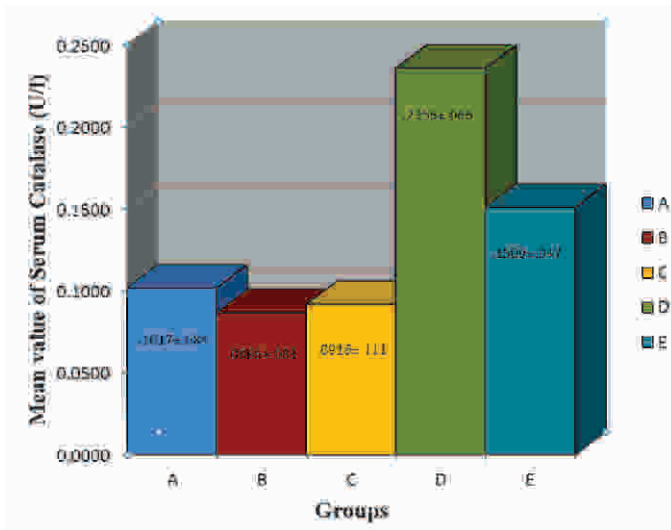


Fig. 1: Bar Chart Showing Comparison of Mean Value of Serum Catalase Among Various Groups

Discussion

PCOS is a condition with significant decrease in serum antioxidant and vitamin levels and there is an increased risk of oxidative stress.¹⁶ Catalase is an intracellular antioxidant that catalyzes the decrease of hydrogen peroxide to water and molecular oxygen and is essentially situated in cell peroxisomes and somewhat in the cytosol.¹⁷ This study shows a significant decrease in the activity of catalase in the disease control group B with PCOS. A deficiency of antioxidants could be due to decrease antioxidant intake, decrease synthesis of antioxidant enzymes, or increase antioxidant utilization. A significant decrease in the catalase activity was similarly reported in PCOS patients as compared to control.^{18,19} These findings are in accordance with our study. Therefore, the decrease in the catalase activity might be due to accumulation of ROS in which enzymatic activity was decreased by the state of oxidative stress in PCOS. Antioxidative supplementation has been shown to improve the PCOS like conditions. The present study assessed the role of antioxidant supplementation (AGE) on testosterone induced polycystic ovaries in prepubertal female rats and serum catalase as oxidative stress marker both in pre-intervention and post-intervention conditions.

After intervention it was clearly seen that there is marked increase in serum catalase enzyme in the group D as compared to other groups. It clearly shows that if polycystic ovaries were there and we treat them with antioxidants, conditions will clearly improve, whereas concomitant use of TP and AGE as in group

C might not improve the conditions of PCOS. The statistical analysis also revealed that if a PCOS like condition was there as in group E, without any intervention its body's own mechanism which improve the condition and produce a small amount of antioxidants to fight with the ROS. This study demonstrates that antioxidants are important in restoring and maintaining the oxidant and antioxidant balance in blood and tissues. It has been found that PCOS is associated with excessive oxidative stress and decreased antioxidant reserves and to improve these conditions we need secondary therapies to prevent the damage.

Conclusion

The involvement of antioxidants (AGE) in the management of polycystic ovaries may be helpful as secondary therapy to prevent the oxidative damage and may be used as a potential approach to overcome this disorder. Various studies have measured antioxidant markers to correlate oxidative stress and polycystic ovaries. This study strongly suggests that oxidative stress has a tremendous role in induction of polycystic ovaries.

Conflict of Interest: None

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Authors Contribution

BY: Conceptionlization of Project

BY,HN: Data Collection

BY,HN: Literature Search

AS: Statistical Analysis

AS: Drafting, Revision

BY: Writing of Manuscript

Discontinuation of Tuberculosis Treatment in Co-Infected TB with HIV

Umer Usman,¹ Muhammad Saqib,² Aneela Chaudhary³

Abstract

Objective: To determine the factors for discontinuation of TB medication in patient with TB/HIV co-infection.

Methods: A cross sectional study conducted in department of pulmonology DHQ hospital, Faisalabad. We analyze the reasons that lead to co-infected TB/HIV patients to discontinue TB medication and to find out the action of health team. Forty-five professionals participated in the study who serves patients with TB/HIV comorbidity. All patients were informed about the procedure.

Result: After compiling the results, it was noted that low socioeconomic conditions, lack of information about the disease, possible side effects are frequent reasons leading to discontinuation.

Conclusion: Global progress in implementation of TB/HIV activities is encouraging but still limited and late. The need of the hour is to strengthen the existing strategies to overcome the current issues.

Keywords: Tuberculosis. Endemic diseases. Acquired Immunodeficiency Syndrome. Patient's refusal to treatment. Patient care team.

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Introduction

Tuberculosis (TB) is an old disease; however, it is still a major public health problem, not only in Pakistan but also worldwide. The increased incidence of TB is related to several factors, including poverty and social inequality, negligence and / or inadequate diagnosis and treatment of new cases, proper information about the disease, demographic variations, and impact of HIV infection. Failure in global TB control due to ineffective control programs has contributed to mortality and multidrug resistance.¹

Pakistan with 179.2 million² population is ranked fifth among the 22 high burden countries.³ Pakistan accounts for 63% of TB cases in eastern Mediterranean region. Total new cases reported were 258251,

composed of 101887 smear positive cases and 112948 smear negative cases. According to WHO report of 2018 total TB cases in Pakistan were 369548, among them new cases were 360472 and 80 % were found to be pulmonary cases.⁴ The highest incidence was in Sindh province while KPK showed estimated 55000 and Baluchistan showed 27000 new cases every year. According to provincial TB control program all type of estimated TB cases was 167799 in Punjab, this area with the highest rate of co-infection with the human immunodeficiency virus (HIV), so the data is more alarming.

TB treatment withdrawal is frequent, becoming a serious problem in Pakistan, especially when this dropout occurs in patients with TB / HIV co-morbidity. Studies conducted in Pakistan showed that dropout rates were ranging from 38%⁵ to 42%.⁶ These rates are extremely high since the Ministry of Health recommends only 5% of dropout as acceptable.⁷ Discontinuation is considered as the patient who after starting treatment ceased to attend the Health Unit for more than thirty consecutive days after the due date for return.⁷ Discontinuation of treatment is considered to be one of the main obstacle and challenge in the fight

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against the disease, with the direct consequence of increasing the cost of treatment, mortality, relapse rates, and facilitating the development of resistant bacillus strains. Generally, factors associated with abandonment are related to the patient, the treatment modality employed and the Health Services.⁸

The conduct of the health team especially in TB with co-infected with HIV, is highly relevant to the success of treatment, aiming to clarify the patients about the nature of their disease, duration of treatment, the importance of regular use of drugs and the serious consequences of stopping treatment. Follow-up with psychologist, supervised doses of medications and monthly bacteriological examinations are team actions that benefit the achievement of cure of TB, enabling greater quality survival for patients with TB / HIV co-infection and avoiding death.

In October 1998, the Ministry of Health launched the National Plan to Combat Tuberculosis (PNCT), bringing among other goals the implementation of the Directly Observed Treatment Short Course (DOTS) strategy which comprises a set of measures defined and recommended by the World Health Organization was the prime focus of treatment. This strategy is based on five pillars: political commitment to TB control, availability of bacilloscopic diagnosis, regular drug supply, efficient Directly Observed Treatment, and Information System. In several countries with cure rates below 50% (China, Peru, Bangladesh) the adoption of this strategy led to increase in cure rates between 80% and 95%.⁹

This research addresses the role of various factors in the discontinuation of TB treatment in patients with TB / HIV co-infection. In HIV-infected patients, health care assistance should be more attentive and careful, as patients need to be encouraged to complete the TB treatment regimen to achieve cure, achieve longer survival, and prevent transmission to others.

Thus, this study aims to analyze through the vision of the health team of a Reference Unit, the reasons that lead TB patients with TB / HIV comorbidity to abandon TB treatment and to know what the team's conduct is in the face of this discontinuation.

Methods

It is a qualitative observational research conducted at the Civil Hospital Rehmat ward Punjab Medical University Faisalabad from 1st of January 2018 to 31st December 2018, where people with HIV and TB

/ HIV co-infection are treated.

Rehmat ward provides care from Monday to Saturday from 8:00 am to 2:00 pm and has been operating for 22 years providing multi-professional assistance, including doctors, nurses, social workers, pharmacists, physiotherapists, occupational therapists, nutritionists, and health technicians. HIV is treated in Allied Hospital Faisalabad.

The research was approved by the Ethics Committee of the hospital.

Forty-five professionals participated in the study: 06 social workers, 09 nurses, 06 doctors, 04 psychologists and 20 nursing technicians who work in the morning and afternoon shifts and serve patients with TB / HIV co-morbidity. The statements were obtained through semi-structured interviews through script of open questions.

The first contact was made with the professionals in the unit inviting them to participate in the research and scheduled interviews with those who agreed to collaborate with it. The interviews were held at the Rehmat Ward itself during their working hours. All were given the free and informed consent form with information about the research objectives and how it would be developed. To respect anonymity and safeguard identification, each interviewee chose a pseudonym, seeking to meet the ethical standards of the research.

The information was worked through the thematic analysis that allows to know a reality through the communications of individuals who are linked to it.

Results

Total of 352 patients were enrolled in the study. Male was predominant with 62% of patients comprising of it. The mean age in our study was 38.6+10 years with highest number of patients between 20 to 30 years of age i.e., 40%, followed by 30 to 60 years 30%. Majority of patients completed the treatment 72.3%, while the remaining who abandoned the treatment most of them were in first month of their treatment (43.9%).

Discussion

As a result of the analysis of the testimonies, two thematic units were constructed for discussion, patient-related factors that make it difficult to adhere to tuberculosis treatment and service-related factors that contribute to the discontinuation of tuberculosis treatment.

1. Patient-related factors that make adherence to tuberculosis treatment difficult

This unit was elaborated from the grouping of some factors related to the patients, which according to the deponents, propitiate the interruption of the treatment, either individual reasons related to the socioeconomic conditions, cultural or those related to the patient, such as drugs side effects, illicit drug use and lack of motivation.

Low socioeconomic conditions were the most frequent reasons leading to the discontinuation of TB treatment which was 60%. Many patients had very low socioeconomic status, sometimes they had no food, and said: "How am I going to take medicine if I have no money to eat?" Socioeconomic factors significantly interfere with the discontinuation of TB treatment. When low socioeconomic factors combine with low education level, the situation worsens by many folds. These factors are manifested in patients' perception of health problems and interfere with their adherence to therapeutic procedures.¹¹

TB drugs side effects appear as the second mentioned factor influencing the discontinuation of TB treatment, either due to minor reactions (nausea, vomiting, diarrhea) or the occurrence of major side effects e.g. drug induced hepatitis. It accounts for 12% of cases regarding discontinuation of treatment. Among this the number of pills (9% of the cause) and side effects of antiretrovirals, associated with the adverse effects of TB drugs facilitated discontinuation. Common side effects that led to medication discontinuation were gastritis, vomiting, diarrhea. Most TB patients are able to complete within the recommended time frame without experiencing any side effects, but when this treatment is associated with antiretroviral treatment, drug interactions and adverse reactions are greater compared to HIV negative subjects. Because of this, it is important to consider that proper adherence in both regimens is a major challenge for the patient when taken concomitantly due to the high number of tablets to be taken daily and the occurrence of side effects, particularly in the first weeks of treatment.¹²

A third important and frequent factor is the use of illicit drugs promoting treatment discontinuation. In our study, it was estimated to be 7% of the cause. Many patients were alcoholics and smokers, so they prefer to get addicted than to take their medication.

2. Service-related factors that contribute to the

discontinuation of tuberculosis treatment.

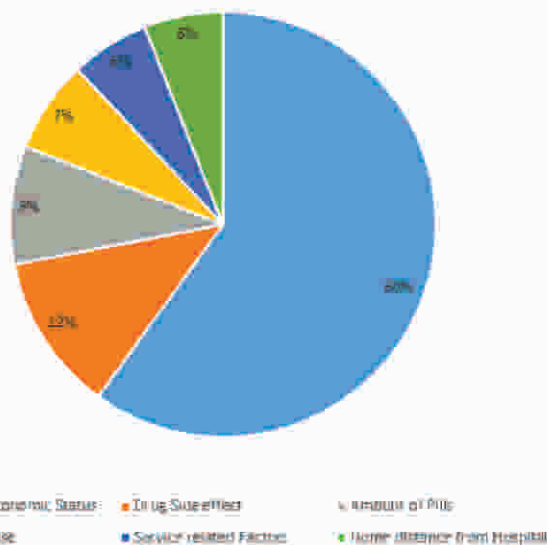
Service-related factors accounts for only 6% of the drop out from treatment. The service-related factors were: little or no information from professionals to the patient about TB treatment, little organization in the service for specific TB control, given that HIV treatment was a priority, physical structure that does not guarantee privacy, absence of teamwork and difficulties in accessing the service.

Lack of information about disease was the commonest complain by the patients and attendees. This lack of information was about the disease, possible side effects, the importance of completing the treatment regimen, even if symptoms improve and the serious consequence of stopping the treatment. Thus, adequate information to the patient and family members about the disease will greatly reduce the likelihood of discontinuation.^{6,14}

Poor organization in the management of TB / HIV cases also contributes to the discontinuation of TB treatment. Here we do not have a structured TB program. Tuberculosis is treated as opportunistic disease, therapy is more ancillary, there is no search for the absentee, when it comes to the HIV consultation, they have already discontinued treatment. Lack of resources was the biggest point raised by the staff there in this regard.

There was no mechanism no strategy to check for adherence to TB treatment. Reason for non-checking the adherence was inadequate space in the building, where supervised treatment would be checked. There are large number of co-infected patients treated at Rehmat Ward Allied Hospital Faisalabad, however there is no physical structure to support this demand, and there are not enough offices to ensure the privacy of both patient and professional, often having to be divided the space for care. In the Rehmat ward this can be minimized by using "Therapeutic Home Care program" consisting of a multi professional health team, with the purpose of providing comprehensive care, bring treatment to patients at their door step who are unable to move to the unit. This strategy can be used to minimize the problem of dropout in cases of TB / HIV coinfection. Using only self-administered treatment increases the likelihood of discontinuation compared to supervised treatment,⁸ because this treatment strategy is an important tool in the fight against TB considering that the patient cannot be solely responsible for their treatment and allows other

Factors leading to treatment Disruption



actors (family, community and health professionals) to participate actively, and it must be done flexibly respecting patients' choices.¹³

Distance was another important factor that hampers adherence. The fact that Rehmat Ward meets most of the district demand also causes many difficulties of access to those residing in the rural areas and especially those who need to move from small municipalities up to DOTS facility. This limited access ends up making it impossible to attend the monthly consultations and evaluations, coupled with this, there are also difficulties to obtain Out-of-Home Treatment for those residing in the rural areas.¹⁴ How a patient who is poor, meager resource, lives far from the place where the treatment center come to treatment by spending money and time? Result is the patients, ends up in discontinuation of treatment thus, making treatment and control difficult.¹⁶

Conclusion

The results of this study point to the need to change the practices developed in the services and patient's perspective. For services related issues changing simple attitudes such as: strengthening existing strategies, encouraging adherence new strategies, following supervised treatment, and seeking more therapeutic possibilities to reduce the unpleasant effects that are potentiated in interactions between antiretroviral and tuberculosis drugs can greatly enhance better outcome. While those related to patients are more difficult to change as they are related to individual vulnerabilities, social and economic factors which are more complex and require governmental actions and health

education through mass media for their change.

Conflict of Interest: None

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Authors Contribution

MSM: Conceptionlization of Project

UU: Data Collection

CA: Literature Search

MSM,CA: Statistical Analysis

UU: Drafting, Revision

UU: Writing of Manuscript

Comparison of Intravenous Magnesium Sulphate and Lidocaine Effects on Attenuating Haemodynamic Variables to Laryngoscopy and Intubation in Patient Undergoing General Anesthesia

Muhammad Azam,¹ Muhammad Wasim Ali Amjad,² Saadia Khaleeq,³ Naila Asad⁴

Abstract

Objective: To determine the effect of intravenous xylocaine and magnesium sulfate on attenuation of hemodynamic response to laryngoscopy and intubation in patients undergoing general anaesthesia.

Methods: This was a randomized controlled study carried out at operation theaters of services hospital lahore after obtaining approval from IRB of hospital. The data was collected over period of six month from 20.05.2020 to 20.12.2020 through electronic databases. 60 patients were divided into two groups of 30 each by lottery method in this randomized control trial. Intravenous magnesium sulphate 30 mg/ kg diluted in 50 ml normal saline 15 min before induction was administered in M group and 50 ml normal saline given in L group. Induction was done with propofol 2 mg/ kg, followed by suxamethonium 2 mg/ kg. I/V lignocaine 1.5 mg/kg diluted in N/S (5ml) was given as bolus in L group and 5 ml N/S IV bolus in M group 1 minute before intubation. Laryngoscopy was performed and the trachea was intubated after 1 minute. HR, systolic (SBP), diastolic (DBP) and mean arterial pressures (MAP) were measured just before securing intravenous access, just before induction, after intubation and 1,3,5 min post intubation.

Results: Mean age for both groups was 36.0±12.8 and 38.2±10.8. Mean HR was significantly different between two groups immediately after intubation (p=0.010), and at 1, 3 and 5 minutes also (p=0.004, p=0.018 and p=0.024) respectively. No significant difference was seen in systolic, diastolic and mean blood pressures at intubation, 1 minute, 3 minutes and 5 minutes after intubation among the groups (p>0.05).

Conclusion: Both Magnesian Sulfate and lignocaine are effective in attenuating haemodynamic response to laryngoscopy and intubation but magnesium sulphate provides better efficacy in control of heart rate.

Key Words: Haemodynamic response, laryngoscopy, Intubation, magnesium sulphate, lignocaine.

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Introduction

Laryngoscopy and endotracheal intubation induces a stress response that occurs due to sympatho-adrenal stimulation.^{1,2,3,4} This pressor response leads to various cardiovascular changes such as increase in heart rate, rise in arterial blood pressure from baseline

and dysrhythmias.² These transient cardiovascular responses may not affect normal healthy individuals but may increase perioperative morbidity and mortality in patients with coexisting disease such as ischemic heart disease, hypertension, cerebrovascular disease and diabetes mellitus.^{1,2}

Several pharmacological and non-pharmacological methods were tried to minimize the adverse sympatho-adrenal response at different times but few were found to be effective. Various drugs like lignocaine, magnesium sulphate, opioids, beta blockers, clonidine, labetalol, calcium channel blockers and vasodilators such as hydralazine have been used.¹

The use of I/V magnesium sulfate 15min before induction of anesthesia provide steady, smooth

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reduction and control of MAP and HR after intubation. This attenuation in hemodynamic response results from the inhibition of catecholamine release from the adrenal medulla and thus indirect vasodilation of blood vessels leading to a decrease in blood pressure. It also has a systemic and coronary vasodilation effect by antagonizing calcium ion in vascular smooth muscle.⁵

2% lignocaine, an amide local anaesthetic, is most widely used to attenuate the stress response to laryngoscopy and intubation when given in dose of 1.5mg/kg intravenously 90 seconds before induction.² The beneficial effect of lidocaine is due to its direct cardiac depression and peripheral vasodilation, ability to suppress airway reflexes as well as antiarrhythmic properties.⁶ Lignocaine decreases airway reactivity by reducing release of substance P and its glycinergic action.⁷

Various studies have been done to compare intravenous magnesium sulphate with lignocaine and other drugs but efficacy is still controversial. The aims of the study to compare the effect of prophylactic use of IV magnesium sulfate with lidocaine on hemodynamics following laryngoscopy and intubation in patients undergoing general anaesthesia.

Methods

This was a randomized controlled study carried out at operation theaters of services hospital Lahore after obtaining approval from IRB of hospital. The data was collected over period of six months from 20.05.2020 to 20.12.2020 through electronic databases. 60 patients scheduled for elective surgery were divided into two groups of 30 each by lottery method. Patients undergoing major head and neck surgeries under general anaesthesia with endotracheal intubation, aged 20-50 years of American Society of Anesthesiologists ASA I and II were included. Patients in whom difficult airway was anticipated, American Society of Anesthesiologists ASA III, patient with raised ICP, IHD, hypertensive and having diabetes mellitus were excluded.

IV access was established with 20G cannula. Baseline heart rate, BP, ECG and Oxygen saturation was recorded. Intravenous magnesium sulphate 30 mg/kg diluted in 50 ml normal saline 15 min before induction was administered in M group and 50 ml normal saline given in L group. All patients were premedicated with nalbuphine 0.1 mg/kg intravenously and induc-

tion was done with propofol 2 mg/kg, followed by suxamethonium 2 mg/kg. I/V lignocaine 1.5 mg/kg diluted in N/S was given as bolus in L group and 5 ml N/S IV bolus in M group 1 min before intubation. A quick and gentle laryngoscopy not lasting for more than 15 second was then performed by one anesthetist and the trachea was intubated. Atracurium 0.25 mg/kg intravenously was administered to maintain anaesthesia using oxygen with isoflurane 1% and IPPV.

Heart Rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial pressures (MAP) were measured just before securing intravenous access (baseline value), just before induction, after intubation and 1,3,5 min post intubation. Hypertension was considered when BP value was greater than 20% of baseline. Hypotension was considered when BP was less than 20% of baseline. Tachycardia was considered when HR was more than 20% of base line or HR greater than 100bpm. Bradycardia was labelled when HR was lower than 50 bpm.

The data for age, weight, SBP, DBP, MAP, and HR were all described by using "Mean±SD". The comparison between two groups at baseline, immediately after intubation, one, three and five minutes after intubation were made by using independent sample t-test. Comparison of each hemodynamic parameter with its baseline value within each group was made by using paired t-test. P-value 0.05 was considered statistically significant. Line graphs were used to present the changes from baseline to 5 minutes after intubation for each parameter.

Results

The mean age for both groups was 36.0±12.8 and 38.2±10.8 which was insignificantly different between two groups, beside this the weight, systolic diastolic and mean arterial pressure were all insignificantly different at baseline with p-values 0.755, 0.877, 0.692 and 0.824 respectively. The heart rate for L group at baseline was 93.0±19.3 and that for M group was 86.7±15.6 and this difference was also insignificant with p-value 0.168. (Table.1)

As the baseline values were all insignificant so direct comparisons were made at each instance at and after intubation between two groups. The systolic, diastolic and mean blood pressures were not found significant at intubation, and 1, 3 and 5 minutes after intubation between two groups. The mean heart rate, however,

immediately after intubation was found significantly different between two groups with p-value 0.010, and at 1, 3 and 5 minutes also were significantly different with p-values 0.004, 0.018 and 0.024 respectively. (table.2)

When compared within group the systolic blood pressure raised a bit from baseline in both groups till

Table 1: Demographic and Hemodynamic Parameters at Start of Study after Randomization

	Group				P-value comparison between groups
	L (n=30)		M (n=30)		
	Mean	SD	Mean	SD	
Age	36.0	12.8	38.2	10.8	0.474
Weight (kgs)	66.6	10.2	67.5	12.7	0.755
SBP	134.3	13.1	133.7	18.0	0.877
DBP	82.7	12.4	83.9	11.6	0.692
MAP	102.2	12.1	102.9	12.3	0.824
HR	93.0	19.3	86.7	15.6	0.168

immediate after intubation but this raise was insignificant. The p-value for immediately after intubation was 0.108 in group L and 0.057 in M. At one 1 minute

after intubation the SBP declined and p-values for two groups were <0.001 and 0.005 respectively. The mean systolic blood pressure reached to 104 mmHg for group L and 105 mmHg for group M at 5 minutes and both were highly significant as compared to baseline with p-values <0.001. (Table.2, fig.1)

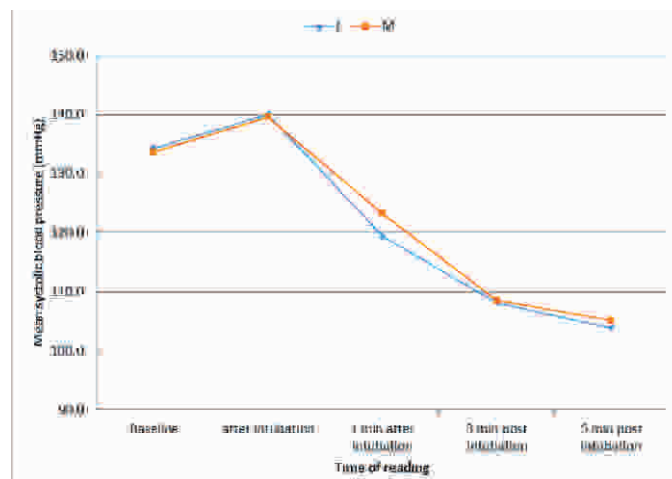


Figure.1: Systolic Blood Pressure for Patients in Two Groups from Baseline to 5 Minutes after Intubation
The pattern for diastolic blood pressure was not diffe-

Table 2: Comparison of Hemodynamic Parameters from Baseline within Group and between Groups at Each Reading Time After Intubation

	Group				P-value comparing two groups
	L		M		
	Mean ± SD	P-value Within group comparison to base line	Mean ± SD	P-value Within group comparison to base line	
SBP					
immediately after intubation	140.1 ± 18.1	0.108	139.6 ± 23.1	0.057	0.931
1min after intubation	119.4 ± 16.9	< 0.001	123.2 ± 15.4	0.005	0.359
3min post intubation	108.2 ± 14.7	< 0.001	108.5 ± 13.1	< 0.001	0.934
5min post intubation	103.9 ± 13.2	< 0.001	105.1 ± 14.6	< 0.001	0.740
DBP					
immediately after intubation	94.6 ± 14.9	0.001	95.1 ± 16.0	< 0.001	0.914
1min after intubation	77.4 ± 12.6	0.054	82.9 ± 16.5	0.762	0.152
3min post intubation	68.0 ± 13.0	< 0.001	70.0 ± 13.7	< 0.001	0.556
5min post intubation	64.0 ± 10.9	< 0.001	66.7 ± 12.4	< 0.001	0.381
MAP					
after intubation	109.7 ± 16.8	0.027	110.3 ± 15.9	0.008	0.881
1min post intubation	92.4 ± 13.1	0.002	94.0 ± 17.1	0.008	0.692
3min post intubation	82.1 ± 13.4	< 0.001	83.1 ± 13.0	< 0.001	0.763
5min post intubation	77.6 ± 11.7	< 0.001	80.2 ± 13.2	< 0.001	0.410
HR					
post-intubation	104.2 ± 13.2	0.003	95.8 ± 11.2	0.003	0.010
1mins after intubation	98.2 ± 13.1	0.099	88.6 ± 11.4	0.504	0.004
3mins after intubation	90.7 ± 14.9	0.402	82.6 ± 10.6	0.107	0.018
5min after intubation	86.0 ± 12.4	0.006	78.6 ± 12.4	0.001	0.024

rent than systolic. It also raised immediately after intubation to 94.6 and 95.1 mmHg in two groups and this raise was significant with p-value 0.001 in L and <0.001 in M group. The decline after one minute was insignificant in group L with p-value 0.054 and in group M with p-value 0.762. Later DBP continued to decline significantly in both groups with p-values <0.001. (Table.2, fig.2)

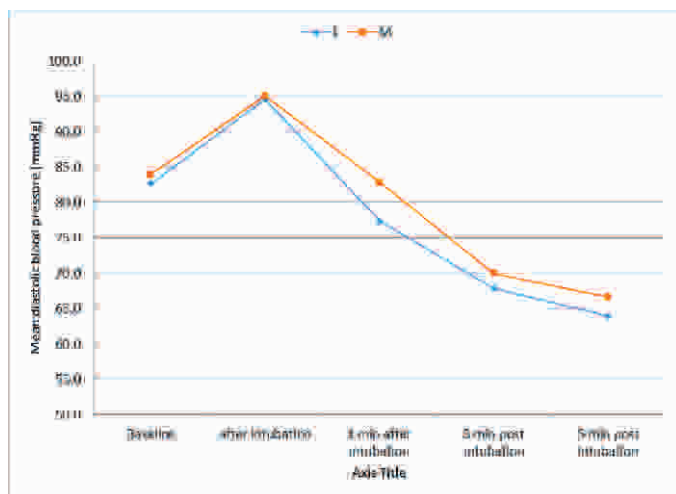


Figure.2: Diastolic Blood Pressure for Patients in Two Groups from Baseline to 5 Minutes After Intubation

The mean arterial pressure increased significantly in both groups immediately after intubation ($p=0.002$ & $p=0.008$) and then declined in both groups significantly at each reading time as compared to baseline. At five minutes the MAP was 77.6 ± 11.7 in group L and 80.2 ± 13.2 in group M. (Table.2, Fig.3)

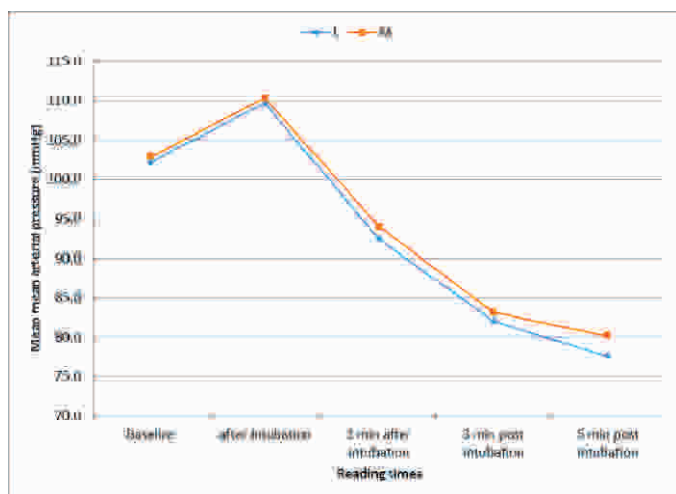


Figure.3: Mean Arterial Pressure for Patients in Two Groups from Baseline to 5 Minutes after Intubation

The heart rate in group L rose to 104.2 ± 13.2 immediately after intubation and this raise was highly

significant with p-value 0.003. In group M the heart rate increased to 95.8 ± 11.2 and this increase was also significant with p-value 0.003. It declined after one minute in both groups but the decline was insignificant in both groups with p-values 0.099 and 0.504 respectively. Even after 3 minutes of intubation the heart rate was insignificantly different in both groups with p-values 0.402 and 0.107. Later, after 5 minutes, the heart rate declined in group L to 86.0 ± 12.4 with p-value 0.006 and in group M to 78.6 ± 12.4 with a p-value 0.001. (Table.2, Fig.4)

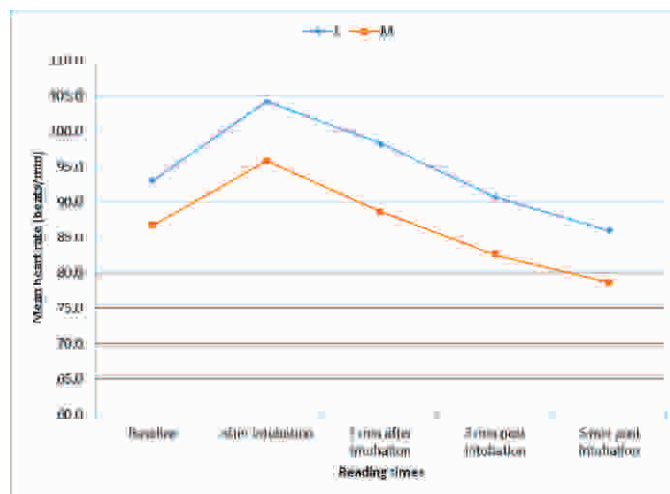


Figure.4: Heart rate for Patients in Two Groups from Baseline to 5 Minutes after Intubation

Discussion

Laryngoscopy and intubation, being noxious stimuli, incite remarkable sympathetic activity. Studies have shown an increase in heart rate with intubation and a greater increase in blood pressure with direct laryngoscopy.⁶ This pressor response, arises 30s after laryngoscopy and intubation and returns to baseline values steadily within 5–10 min. These transitory responses usually produce no consequences in healthy individuals but may be harmful to the patients having reactive airways, hypertension, coronary artery disease, myocardial insufficiency and cerebrovascular diseases.¹

Common factors precipitating the pressor response to laryngoscopy and intubation are light planes of anaesthesia, prolonged time for the procedure, elevation of vagally innervated posterior part of epiglottis by straight/ Miller blade, anatomically difficult view, greater force used to displace the tongue and more manipulations/ attempts at laryngoscopy and intubation. Several drugs and maneuvers have been used for mitigating this stress response with variable benefits and side effects.

Magnesium Sulphate and lignocaine 2% appear to meet the characteristic of a drug to prevent these sympathetic response. Comparison of magnesium sulphate with lignocaine in our study did not show significant difference in systolic, diastolic and mean blood pressures at intubation, 1 minute, 3 minutes and 5 minutes after intubation among the groups ($p > 0.05$). However, the mean heart rate decreased significantly in Magnesium group after 1, 3 and 5 minutes of intubation when compared to Lignocaine ($p = 0.01$, $p = 0.00$, and $p = 0.02$).

In 2017, Bhalerao NS showed similar result to our study as there was no significant increase in BP after laryngoscopy when compared with base line with use of intravenous MgSO₄ 50 mg/kg and lignocaine 2mg/kg in hypertensive patients.⁸

In accordance to our study, Rajan Sunil observed there was a statistically significant decrease in HR from the pre-induction values in MgSO₄ group (50mg/kg) than lignocaine group up to 15 min following intubation. Although there was decrease in systolic blood pressure, diastolic blood and mean arterial pressure from induction values in both groups, there was no significant difference between the groups.⁹

Kiaee M et al concluded similar results regarding heart rate changes when comparing magnesium sulphate with lignocaine. Difference in results were shown in systolic, diastolic and mean arterial pressures. In contradiction to our study results they found greater decrease in systolic, diastolic and mean arterial pressures with lignocaine.⁵

Padmawar S in 2016 found comparable results to our study. The difference in attenuation of heart rate was significant among groups but no significant difference was seen in SBP, DBP and MAP in comparison of lignocaine and magnesium sulphate groups at intubation, 1 minute, 3 minute and 5 minutes after intubation. Magnesium sulphate group was found better than lignocaine.²

Consistent with our results, significant fall in heart rate was noted by Vallabha et al following induction, laryngoscopy, and intubation when comparing magnesium (30mg/kg) with lignocaine (1.5mg/kg) group. The decrease in mean arterial pressure was significant unlike the results of our study.³

Nooraei N et al used 60mg/kg magnesium sulphate and lignocaine 1.5mg/kg in 60 patient and concluded

there was significant decrease in heart rate with lignocaine at 3rd and 4th minutes after intubation that were contrary to our results. But similarity was seen in the results of systolic, diastolic and mean arterial pressures with no significant difference among both groups.¹⁰

In 2017 CCRGA evaluated 56 patient and found different result from our study. There was increase in heart rate and blood pressure after laryngoscopy and intubation compared to baseline. The reason may be they used bispectral index in their study to assess the depth of anesthesia which is not used in our study.

In 2011 SH Majid Waseem et al found different result from our study. They found lignocaine was more effective and efficacious than magnesium sulphate. In 89 patients they used intravenous 1% lignocaine 1mg/kg and magnesium sulphate 10 mg/kg instead of 1.5mg/kg lignocaine and 30mg/kg magnesium sulphate intravenous in our study.¹¹

We did not monitor depth of anaesthesia due to unavailability of Bispectral Index and also used suxamethonium for intubation instead of non-depolarizing muscle relaxant. In future, research can be planned to evaluate these limitations of our study.

Conclusion

Both Magnesian Sulfate (30mg/kg) and IV lignocaine (1.5mg/kg) are effective in attenuating haemodynamic response to laryngoscopy and intubation without any deleterious effects. However, magnesium sulphate provides better efficacy in control of heart rate.

Conflict of Interest: None

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Diagnostic Accuracy of Ultrasonography in Diagnosing Morbidly Adherent Placenta, Taking Intra-Operative Findings as Gold Standard

Anum Yousaf,¹ Misbah Durrani,² Khoala Riaz,³ Ume Kalsoom,⁴ Hassan Parvez⁵

Abstract

Objective: Various imaging modalities can be employed for the placenta accreta diagnosis like USG and MRI, however, their exact diagnostic accuracy is yet to be established. This study was conducted for determining the accuracy of ultrasonography in diagnosing morbidly adherent placenta in women with a previous scar, taking the per-operative findings as gold standard.

Methods: This descriptive cross-sectional study was carried out at department of Radiology, Benazir Bhutto Hospital, Rawalpindi from 6th January 2019 to 5th July 2019. Using non-probability purposive sampling 118 pregnant women with single pregnancy of age 18-40 years were included. Both grey scale and color doppler findings of ultrasound were employed for ascertaining presence or absence of morbidly adherent placenta. Per-operative findings of all patients who underwent cesarean section afterwards in their respective wards were registered. The findings of USG were then compared with the per-operative observations.

Results: Among patients in whom USG findings were of morbidly adherent placenta, 60 were true positive while 05 were false positive, whereas, in the patients with no evidence of morbidly adherent placenta on USG, 03 were false negative while 50 were true negative. The sensitivity, specificity, positive predictive value negative predictive value and diagnostic accuracy of USG in diagnosing morbidly adherent placenta in previous scar women, taking per-operative findings as gold standard was 95.24%, 90.91%, 92.31%, 94.34% and 93.22% respectively.

Conclusion: It can be inferred from our study that USG is a very sensitive and accurate non-invasive imaging technique for the diagnosis of morbidly adherent placenta.

Keywords: morbidly adherent placenta, ultrasonography, sensitivity.

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Introduction

The term “morbidly adherent placenta” is used to denote an abnormal attachment of placenta. It can either be accreta, increta or percreta as per its depth of invasion. The increased cesarean rate in the world is the main culprit of increasing incidence of morbidly adherent placenta.¹ A recent study

conducted by WHO which included 137 countries found that 69 nations had rates of cesarean sections above 15% whereas a significant number of countries had this rate as high as 30-35%.² These high rates of cesarean sections world-wide are associated with a number of complications and constitute a significant proportion of maternal morbidity and mortality rate.³ These complications include massive hemorrhage, need for large volume transfusions, infections, ureteral and bladder damage, ICU admissions and ventilation. With a view to over-come these complications the overall management of pregnancy has been improved significantly from time to time including an update of antenatal diagnostic approach and perioperative strategies.⁴

Prenatal diagnosis is essential for appropriate

- | | |
|------------------|-------------------|
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counseling and surgical planning to be performed. A confirm diagnosis of placenta accreta can only be made on pathological basis after hysterectomy. Visualization of chorionic villi extending to myometrium with no decidual layer in-between on the histological sample confirms the diagnosis.

Various imaging modalities can be employed for the placenta accreta diagnosis like USG and MRI, however, their exact diagnostic accuracy is yet to be established and is mainly operator dependant.⁵ The features of adherent placenta on ultrasonography are numerous vascular spaces within placenta, no retro-placental clear or hypo-echogenic zone, interrupted bladder wall and thin myometrium as shown in figure I.⁶

This study was conducted for determining the accuracy of ultrasonography in diagnosing morbidly adherent placenta in women with a previous scar, taking the per-operative findings as gold standard. This will not only highlight the local stats of the USG diagnostic accuracy in morbidly adherent placenta but also these particular patients can be provided with a non-invasive imaging modality for accurate prenatal identification of morbidly adherent placenta. Moreover, it will also help clinicians for optimal obstetric management.

Methods

This descriptive cross-sectional study was carried out at department of Radiology, Benazir Bhutto Hospital, Rawalpindi from 6th January 2019 to 5th July 2019. Using non-probability purposive sampling 118 pregnant women of age 18-40 years with singleton pregnancy with history of one or more cesarean sections were included after ethical approval of the study from the ethical review board of Rawalpindi Medical University. After taking informed consent, ultrasound was done by Doppler ultrasound machine using 3.5 MHZ curvilinear transducer. Both grey scale and Color Doppler findings of ultrasound were noted and interpreted collectively under supervision of a classified radiologist and presence or absence of morbidly adherent placenta was ascertained. Then intra-operative findings of all patients who underwent cesarean section in the concerned ward were noted. USG findings were compared with the operative findings.

Age, gestational age, parity and number of previous cesarean sections were presented as mean and standard deviation. Morbidly adherent placenta on USG and intra-operative findings were presented as frequency

and percentage. Collected data was analyzed through computer software SPSS 23.0.

Results

The mean age of patients in our study was 28.64 ± 3.87 years with a range of 18-40 years. About three fourth of the subjects 89 (75.42%) were between 18 to 30 years of age. The mean gestational age was 38.55 ± 1.22 weeks with a mean parity of 2.25 ± 0.64 . Whereas, the mean number of previous cesarean sections was 1.24 ± 0.64 . All of this is summarized in Table I.

Ultrasound of all the subjects was done by a qualified sinologist having appropriate training in this regard. USG showed the morbidly adherent placenta in 65 (55.08%) patients. Operative findings confirmed morbidly adherent placenta in 63 (53.39%) cases where as 55 (46.61%) patients revealed no morbidly adherent placenta. In USG positive patients, 60 were true positive while 05 were false positive. Among, 53 USG negative patients, 03 were false negative while 50 were true negative as shown in Table II.

Table 1: Demographics and Other Characteristics of the Patients

Parameters	Mean \pm SD
Age	28.64 \pm 3.87 years
Gestational Age	38.55 \pm 1.22 weeks
Parity	2.25 \pm 0.64
Cesarean section	1.24 \pm 0.64

Table 2: Table II: Diagnostic Accuracy of Ultrasonography (USG) in Diagnosing Morbidly Adherent Placenta in Previous Scar Women, Taking Intra-Operative Findings as Gold Standard

USG Findings	Positive result on Surgery	Negative result on surgery
Positive result on USG	60 (TP)	05 (FP)
Negative result on USG	03 (FN)	50 (TN)

TP= True Positive, FP= False Positive, FN= False negative, TN= True Negative

Table 3: The Sensitivity, Specificity, PPV, NPV and DA of USG in Diagnosing Morbidly Adherent Placenta

Parameters	Sensitivity	Specificity	PPV*	NPV**	Dv***
Value	95.24	90.91	92.31	94.34	93.22

*Positive Predictive Value, **Negative Predictive Value, ***Diagnostic Accuracy

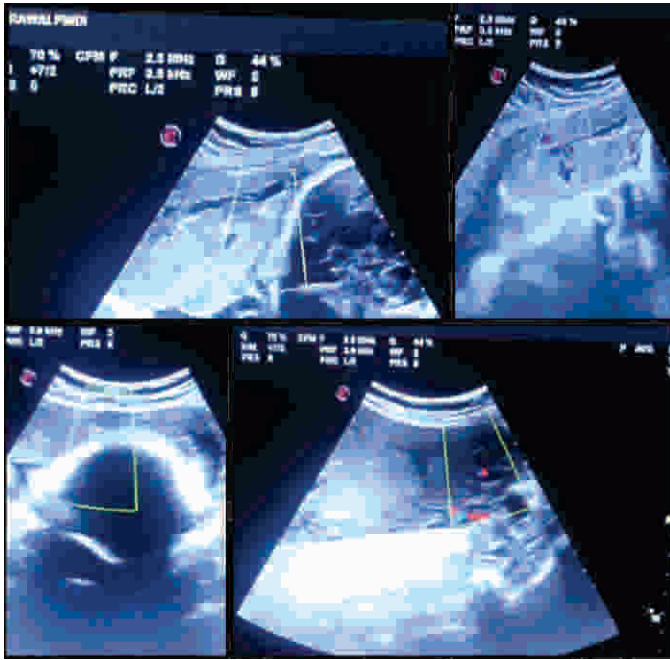


Figure 1: Normal Appearing Placenta Showing Maintained Retroplacental Hypoechoic Zone and No Significant Vascularity or Placental Lacunae in the Upper Half. In the Bottom Half, Marked Thinning of Retroplacental Hypoechoic Zone with Placental Lacunae and Vascularity is Evident

Overall sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of ultrasonography (USG) in diagnosing morbidly adherent placenta in previous scar women, taking intra-operative findings as gold standard was 95.24%, 90.91%, 92.31%, 94.34% and 93.22 respectively. This is summarized in table III.

Discussion

Morbidly adherent placenta is one of the biggest causes of maternal illness and death and can be regarded as the commonest cause of hysterectomy after delivery now a days. Placenta previa and previous history of cesarean sections are the major predisposing factors with the risk increasing as high as 50% with a history of 3 or more previous cesarean sections.^{7,8} An abnormality of the decidua basalis allows the chorionic villi to invade the myometrium. It is classified into 3 sub-types as per degree of invasion i.e. placenta accreta, placenta increta and placenta percreta. The most common type is the placenta accreta in which the villi attach to the myometrium of uterus but do not invade it. The second most common type is placenta increta in which the villi penetrate into the myometrium, however, invade it partially. The least common and the most severe form of morbidly adhe-

rent placenta is the placenta percreta in which the villi passes through the entire uterus and placenta may be seen attached to the nearby organs like bladder.

In our study, overall sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of ultrasonography (USG) in diagnosis of morbidly adherent placenta in previous scar women, taking per-operative findings as gold standard was 95.24%, 90.91%, 92.31%, 94.34% and 93.22% respectively. These results are in line with many of the previously conducted studies on the same topic. In a study, prevalence of morbidly adherent placenta was found to be 28.0% and sensitivity and specificity of ultrasonography in diagnosing morbidly adherent placenta as 85.7% and 83.3% respectively.⁹ In another study, sensitivity and specificity of ultrasonography in diagnosing morbidly adherent placenta was found to be 50.8% and 86.4% respectively.¹⁰

Ultrasonography is the first investigation of choice for assessment of placenta and its position. The transvaginal ultrasound has a sensitivity of 77% to 87% and specificity of 96% to 98% to detect an adherent placenta as per American College of Obstetrics & Gynecology. In addition, Positive Predictive Values (PPV) and Negative Predictive Value (NPV) reported are 65% to 93% and 98%, respectively.¹¹

Similarly, a local study showed sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of Doppler ultrasound in detecting morbidly adherent placenta as 87.5%, 98.36%, 87.5%, 98.36% and 97.10% respectively.¹²

Conclusion

This study concluded that ultrasonography is a very sensitive and accurate method of detecting a morbidly adherent placenta, and not only greatly improves our ability to detect it but also improves patient care through accurate diagnosis and timely devising appropriate intra-operative strategies. Therefore, being risk-free and a very sensitive diagnostic tool, we should recommend it as a primary diagnostic tool to accurately identify the placental abnormality in these patients in order to reduce maternal morbidity and mortality.

Conflict of Interest: None

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Authors Contribution

YA,DM: Conceptionlization of Project

YA,DM,RK: Data Collection

DM,RK: Literature Search

RK,KU: Statistical Analysis

KU,PH: Drafting, Revision

YA,DM,PH,KU: Writing of Manuscript

Low Sodium Levels in Children Affected with Community Acquired Pneumonia

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Abstract

Objective: The objective of this study is to find out whether subjects who are suffering from community acquired pneumonia also had low sodium levels.

Methods: One hundred children fulfilling our criteria and admitted in Department of Pediatrics, Services Hospital, Lahore were included in the study. Five cc venous blood was drawn from each children of community acquired pneumonia and sent to hospital laboratory for evaluation of blood sodium levels.

Results: one hundred cases of CAP were included in the study. When mean +SD of age was calculated, mean age of the study population was found to be 1.55+0.52 years. In addition, 55 % (n=55) were male while 45 % (n=45) were females. 27 % (n=27) children effected with CAP were found to be having low sodium levels whereas 73 % (n=73) had normal sodium levels.

Conclusion: After conducting research, we have come to the conclusion that community acquired pneumonia is very frequent among children in the age group between 1-1.5 years. If it is promptly treated, children can be saved from life threatening pathologies.

Key Words: Children, community acquired pneumonia, hyponatremia

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Introduction

Community-acquired pneumonia (CAP) is a major problem all over the world but its incidence is much higher in the underdeveloped world. More than one million children die from pneumonia every year. Major cause of pneumonia is viral in origin. Respiratory syncytial virus, influenza A, and parainfluenza types 1 through 3 are the most common viral agents. It is followed by infection with bacteria's like streptococcus pneumonia.^{3,4}

Most of the cases of CAP, resolves on its own but if left untreated it is associated with many complications including that of renal system. The measurement of serum electrolytes may be helpful in assessing the degree of dehydration in children with limited fluid intake and whether hyponatremia is present.⁵ Many studies have produced a positive relationship between respiratory tract infections and hyponatremia.⁶ A study reported an incidence of 27.9% hyponatremic children who had CAP. Similarly, Don M and colleagues have found 45% incidence of hyponatremia in children of CAP. HN is easy to diagnose and rarely dangerous, but sometimes its origin may be difficult to settle, and inappropriate fluid therapy may lead to complications.⁷ Hyponatremia is defined as a serum sodium <135 meq/L, the most common disorder of body fluid and electrolyte balance encountered in clinical practice. Moderate hyponatremia if the serum Na concentration is between 125 and 129 meq/L. Severe is the serum sodium concentration is less than 126 meq/L.⁶ Hyponatremia results from water retention or shift of sodium from intracellular to extracellular fluid or vice versa.⁸ The syndrome of inappropriate

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antidiuretic hormone (SIADH) which is common in many paediatric illnesses of pulmonary, cerebral or malignant origin is responsible for water retention and thus causes hyponatremia.⁹

The rationale of the study is that no local literature is available to address this issue while international studies are showing a significant difference which needs another study to be conducted in our local population so that the actual frequency of the morbidity may be determined which will be helpful for the paediatricians for timely prevention of complications of hyponatremia e.g. increased hospitalization stay, cerebral edema, seizures, coma and death in community acquired pneumonia.

Methods

A Cross sectional Study was carried out in the Department of Paediatrics, Services, Hospital, Lahore. Children of age up to 2 years who are diagnosed as cases of CAP in the last 72 hours. However, already diagnosed cases of hyponatremia (on history and medical record), Children having previous history of hyponatremia (on history and medical record) and children who were not willing to participate were excluded from the study. Informed consent of the parents of children was obtained to include their data in the study. The demographic profile of every children was recorded. 5cc blood sample of children who were diagnosed with CAP was taken and sent to hospital lab and was checked by spectrophotometric method. The data was analyzed through IBM SPSS version 22. Mean \pm SD were calculated for age. Stratification for age, gender, duration of CAP, nutritional status (i.e. malnourished/nourished) and socio-economic status were done to control the effect modifiers. Post stratification chi-square test was applied to know the significance. p value <0.05 was considered as significant.

Results

A total of 100 cases fulfilling the inclusion/exclusion criteria were enrolled. Subjects were than stratified according to their age. Mean + SD age was calculated as 1.55+0.52 years. In addition, it showed that 45% (n=45) had up to 1 year of age while 55% (n=55) were between 1-2 years of age. Gender distribution shows that 55 % (n=55) were male while 45 % (n=45) were females. Frequency of hyponatremia in children with community acquired pneumonia was recorded in

27% (n=27) whereas 73 % (n=73) had no findings of the morbidity. (Table no. 1) Frequency of hyponatremia with regards to age showed that 7 out of 45 cases up to 1 year of age and 17 out of 55 cases between 1-2 years of age had hyponatremia. p value was 0.07. (Table No. 2). Stratification for frequency of hyponatremia with regards to gender shows that 12 out of 55 male and 12 out of 45 female cases had hyponatremia,

Table 1: Frequency of Hyponatremia in Children with Community Acquired Pneumonia (n=100)

		Hyponatremia		p-value
		Yes	No	
Age	Up to 1 year	7	38	0.07
	1-2 year	17	38	
Gender	Male	12	43	0.42
	Female	12	33	
Duration of CAP	1-2 weeks	18	49	0.33
	>2 weeks	6	27	

Table 2: Stratification for Frequency of Hyponatremia with Regards to Age, Gender and Duration of Community Acquired Pneumonia (n=100).

Hyponatremia	No. of patients	%
Yes	27	27
No	73	73
Total	100	100

p value was 0.42. Frequency of hyponatremia with regards to duration of CAP shows that 18 out of 67 1-2 weeks duration of CAP and 6 out of 33 >2 weeks duration of CAP had hyponatremia, p value was 0.33. (Table No. 2)

Discussion

Hyponatremia is the most common finding in children of community acquired pneumonia. The current study was planned with the view that no local literature is available to address this issue while international studies are showing a significant difference. Hyponatremia leads to severe life threatening complications like cerebral edema, epileptic fits, coma and even death. The rationale of the study is to find out the frequency of hyponatremia in our population so that physicians can be guided accordingly.

In our study, we found out that frequency of hyponatremia in children with community acquired pneumonia was 24 %. A study done by Wrotek A and others recorded hyponatremia in 33.3% cases of CAP.⁶ Another study recorded these findings (i.e. hyponatremia) in 27.9% of the cases (with community acquired pneumonia).⁷ The findings of our study are in agreement

with the above studies, while another study recorded it in 45.4% of children with community acquired pneumonia.¹⁰ These findings are higher than our results and can be explained by the fact that they have included patients having all type of respiratory infections whereas we have included only those patients who are suffering from lower respiratory tract infection i.e., pneumonia.

When hyponatremia was stratified with age, gender and duration of disease, it should positive statistical significant result with age only. These results were in line with a study conducted by Mandal and colleagues.¹²

Hyponatremia is usually mild in children with CAP.¹¹ The basic pathophysiologic mechanism behind this can be explained by considering the role of two hormones which are antidiuretic hormone (ADH) and atrial natriuretic peptide (ANP).¹⁰ Atrial natriuretic peptide is produced from atrial muscles. It is a natriuretic peptides. It regulates arterial pressure by regulating diuresis and natriuretic.¹³ Fever or dehydration reset the osmostat for ADH secretion, in addition it increase atrial natriuretic peptide secretion. Over-secretion of ANP is correlated with hypoxia, which leads to pulmonary vasoconstriction, pulmonary hypertension, and right-heart overload.^{11,12} Garrahy et al.¹³ found that 68% of hyponatremia in community acquired pneumonia had characteristics typical of SIADH.

Severe hyponatremia is rare in children with CAP. This can be explained by the observations of Haviv et al which reported that ANP helps to maintain sodium level within normal limits through its diuretic and natriuretic effect.¹⁴ In addition, Gerigk et al.,¹⁵ found that ADH may cause HN that may originate by a non-osmotic, cardiovascular mechanism in acutely ill children, including children with pneumonia.

Hyponatremia, the most common frequent electrolyte derangement identified among hospitalized patients¹⁶ and is associated with worsened clinical and economic outcomes and indicates a poor prognosis.¹⁷ It is important to emphasize that the presence of HN is associated with not only prolongation of hospitalization, but also with an increase in hospital mortality.¹⁸ In our study, children with HN at admission had longer hospitalization times and a prolonged duration of fever, although their final outcome was favorable, including cases that developed pleural effusion.¹⁷

The point to ponder is whether hyponatremia in most patients is simply a powerful marker of severity of the underlying disease or a direct contributor to the adverse outcomes observed. But whatever it may be, hyponatremia is a compelling independent marker of adverse outcome.¹⁹ The danger of fluid overload in children with bacterial meningitis is widely appreciated²⁰, but it has not been valued how commonly fluid restriction is indicated in pneumonia in childhood.¹⁷ An Indian study concluded that fluid therapy in pneumonia should be modified. Those having hyponatremia with hyper osmolality need liberal fluids while those with hypo osmolality need fluid restriction and hypotonic fluids.²¹ In the end, we think that more studies with greater sample size and prolonged duration of research are needed to explore the mechanism and association of hyponatremia with severity of illness.

Conclusion

We came to a conclusion that hyponatremia is common among children affected by pneumonia and should be kept in mind while treating for pneumonia. But it needs more prolonged studies to find whether hyponatremia levels are associated with severity of disease or not.

Conflict of Interest: None

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Stress, Resilience and Moral Distress among Health Care Providers During COVID-19 Pandemic

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Abstract

Objective: This study aims to determine level of stress, resilience and moral distress among health care providers during covid-19 pandemic.

Methods: This is a cross-sectional study performed using an online questionnaire.

Data was collected from Health Care Providers, working in various tertiary care hospitals of Lahore, using an online questionnaire. Perceived stress scale (PSS), Connor-Davidson Resilience Scale (CD-RISC 10) and Moral Distress Thermometer were used to determine level of stress, resilience and moral stress respectively among the HCPs. Scores on the PSS can range from 0 to 40 with scores of 0-13, 14-26 and 27-40 being considered as low, moderate and high stress respectively. The Moral Distress Thermometer has scores ranging from 0-10 with value of ≥ 4 considered high. Data was analyzed using SPSS version.23. Descriptive variables were reported as means and frequencies. Intergroup analysis was done using Chi square test with $p < 0.05$ taken as significant.

Results: A total of 278 (n=278) HCPs participated in study. According to the PSS (Perceived Stress Scale) scores, 5.03% (14) reported low, 86.69% (241) moderate and 8.27% (23) high stress levels. The mean stress score is 21.56 \pm 4.32.

Providing patient care (mean = 2.28 \pm 1.15 SD) and transmitting infection to others (mean = 3.02 \pm 1.10 SD) were deemed major causes of stress. The mean CD-RISC score was 23.14 \pm 7.81 SD. Only 10.8% (30) had a score of ≥ 32 . The mean Moral Distress score was 4.2 \pm 2.98 SD, with 53.2% (149) participants reporting high Moral distress (score ≥ 4).

Conclusion: The high level of stress among HCPs during COVID-19 pandemic highlights the need of urgent measures to overcome this psychological issue which if left un-addressed can affect performance of HCPs.

Key Words: Stress, Resilience, HCPs

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Introduction

COVID-19 is an infectious disease of the respiratory tract caused by the SARS-COV-2. Originating in fish markets of Wuhan, China in the December

of 2019, it has since become a global pandemic with more than 40 million cases and almost 1 million deaths. The common symptoms include fever, cough, shortness of breath, fatigue, new loss of sense of smell and taste and sometimes no symptoms at all. The disease mainly spreads via respiratory droplets among people who are in close proximity.¹

HCPs (Health-Care Providers) typically face many stressors related to care for patients with different diseases. Especially in Pakistan, some of these include long working hours, high intensity shifts, non-availability of resources to provide the highest level of care and poor administration and management. Many of these lead to increased level of stress, anxiety, depre-

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ssion and lower levels of resilience among the HCPs.² Although all HCPs face such challenges to some extent, their magnitude varies across different specialties. Recently, COVID-19 has been an additional source of stress and moral distress among the HCPs. From the fear of getting the infection to the stress of transmitting it to others, it has been a source of constant distress for the HCPs.

Stress, resilience and moral distress are the 3 parameters discussed in this study.

Stress can be defined as the degree to which you feel overwhelmed or unable to cope as a result of pressures that are unmanageable.³

Resilience is understood as referring to positive adaptation, or the ability to maintain or regain mental health, despite experiencing adversity.⁴

Moral distress is the painful psychological disequilibrium that results from recognizing the ethically appropriate action, yet not taking it, because of such obstacles as lack of time, supervisory reluctance, an inhibiting medical power structure, institution policy, or legal considerations.⁵

Methods

This is a cross-sectional study performed using an online questionnaire

Data was collected from Health care professionals (HCPs) working in various tertiary care hospitals of Lahore, using online questionnaire.

For stress, The Perceived Stress Scale (PSS) (Cohen, Kamarch, & Mermelstein, 1983) has been used to assess the stress levels among the HCPs.⁶ To make the study easier for the participants, the recall-period has been shortened to 7 days. Scores on the PSS can range from 0 to 40. Scores ranging from 0-13 would be considered low stress. Scores ranging from 14-26 would be considered moderate stress. Scores ranging from 27-40 would be considered high perceived stress.

In addition, we have added seven items (stress due to work environment, patient care, personal safety, and indirect sources [home life, social isolation, other restrictions) with respect to the current COVID-19 pandemic. Each item is scored on a scale of 0-4, and mean stress scores were calculated.

For resilience, The Connor-Davidson Resilience Scale (Connor, K. M., & Davidson, J. R., 2003) has been used.⁷ For our purposes, we have used the CD-

RISC 10 that includes 10 items.⁸ In the general population, a median score of 32 was determined (Campbell-Sills et al., 2009) with the lowest to highest quartiles being 0-29, 30-32, 33-36, and 37-40.⁹

The Moral Distress Thermometer (Wocial, L.D. & Weaver, M.T., 2013) has been used as the tool to assess moral distress among the HCPs (10). In a recent validation study, the threshold for high score was considered to be 4 (or higher).

This is a cross-sectional study performed using an online questionnaire. Our target population for this study were the HCPs working in multiple departments of different tertiary care hospitals in Pakistan. The questionnaire included the above-mentioned standard scales and assessment criteria. The data has been analyzed using SPSS ver. 26. Quantitative variables like age, resilience and moral distress scores have been described in terms of their mean values and ranges. Stress, resilience and moral distress scores have also been assessed in terms of percentages and frequencies and have been compared with variables like gender, age etc using chi square test ($p=0.005$).

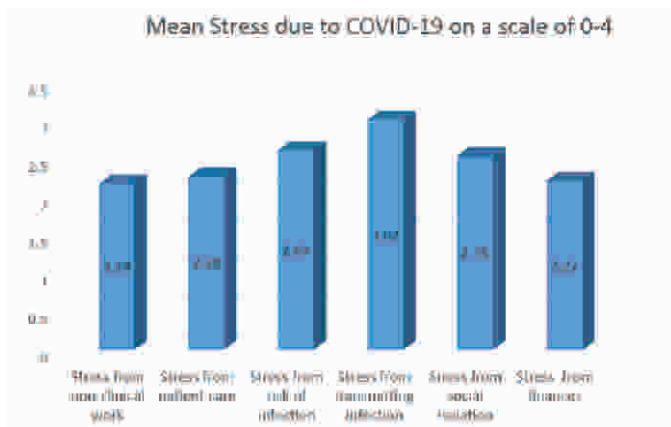
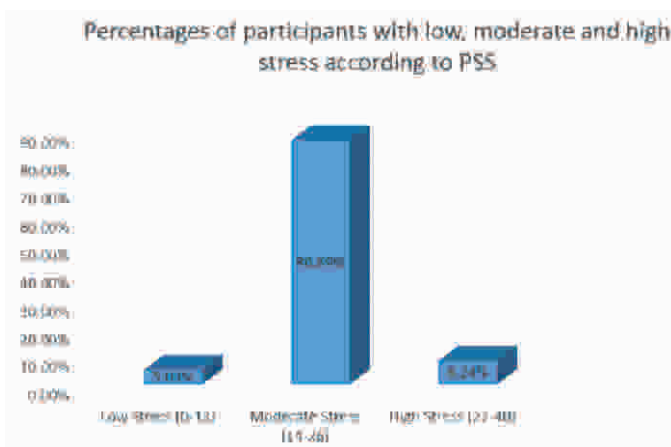
Results

A total of 278 ($n=278$) participants took part in the study with ages ranging from 22 to 54 (mean age = 25.47 ± 3.71 SD). 113 (40.6%) were males and 165 (59.4%) were females with majority of the subjects being single (237; 85.3%). Out of the 278 participants, 265 (95.3%) were practicing doctors while the remaining belonged to other fields. 101 (36.33%) belonged to Surgery and allied while the remaining 177 (63.66%) belonged to Medicine and allied.

According to the PSS (Perceived Stress Scale) scores, 5.03%¹⁴ of the participants reported low stress levels, 86.69% (241) reported moderate and 8.27%²³ reported high stress levels. The mean stress score is 21.56 ± 4.32 SD. Moreover, providing patient care was more stressful (mean = 2.28 ± 1.15 SD) as compared to stress that came from daily non-clinical work routine (mean = 2.18 ± 1.09 SD). Similarly, transmitting the COVID-19 infection to others was deemed to be a greater cause of stress (mean = 3.02 ± 1.1 SD) by the participants as compared to contracting the infection themselves (mean = 2.62 ± 1.27 SD). Mean stress level from the need for social isolation was 2.55 ± 1.44 SD and mean stress from financial problems was 2.22 ± 1.44 SD.

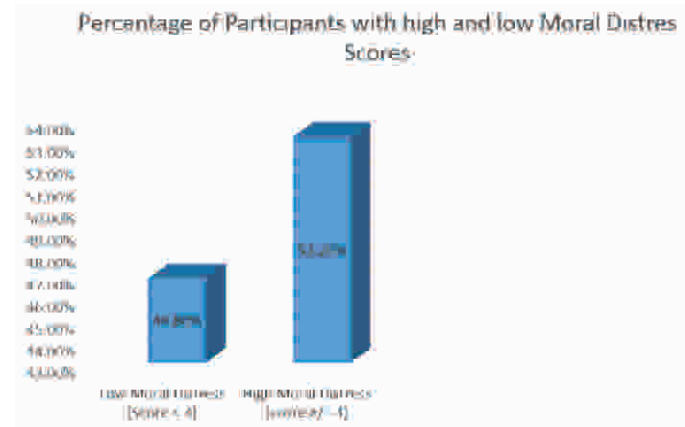
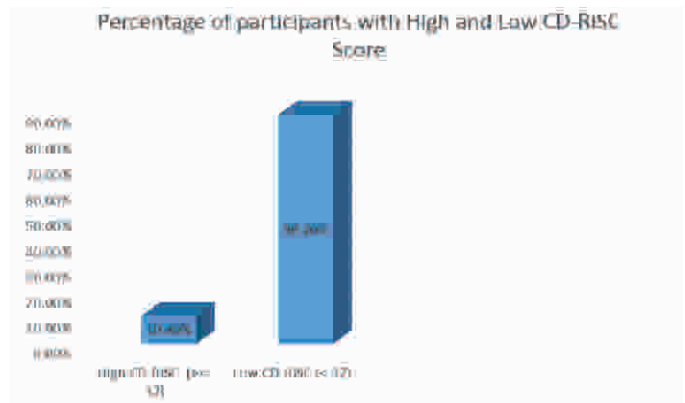
Table 1:

	Demographics	Count	Percentage
	Total Participants	n=278	100
Gender	Male	113	40.6
	Female	165	59.4
Marital Status	Single	237	85.3
	Married	41	14.7
Profession	Doctor	265	95.3
	Others	13	4.7
Department	Medicine and Allied	177	63.66
	Surgery and Allied	101	36.33
Age	25.47+/-3.7 (range=54-22=32)		
No. of family members	5.87+/-1.87 (range=16-2=14)		



The mean CD-RISC (Connor Davidson Resilience Scale) score for all the participants was 23.14+/-7.81 SD. Only 10.8%³⁰ of the participants had a CD-RISC score of 32 or above.

The mean Moral Distress score was 4.2+/-2.98 SD, with 53.2% (149) participants reporting high levels of Moral distress (score ≥ 4).



Discussion

COVID-19 has emerged as one of the biggest threats to mankind during the recent times. It has affected every aspect of human life. Public health has been its primary target.

One aspect of public health that is ignored most of the times is the issue of mental health. Healthcare services, by their nature, tend to be mentally and psychologically exhausting for the providers. Doctors, in general have lower levels of resilience in comparison to the normal population. Similarly, doctors of emergency medicine in particular, due to high workload and nature of their work, are more prone to burnout as compared to other specialties of medicine.¹¹

During these hard times of COVID-19, when there is air of fear and uncertainty, the psychological and mental health of the individuals has been more severely affected. There is increased stress, depression and anxiety, even among the general population.¹² Health Care Providers are the first line of defense against this pandemic. Naturally, they are the ones that are the most susceptible to its hazardous effects, both physically and psychologically.¹³

Previous literature suggests that the HCPs treating patients with COVID-19 reported higher levels of anxiety and low self-efficacy levels.^{14,15} Other studies on Wuhan medical professionals reported greater

susceptibility to stress, anxiety, and depression, suggesting that the mental health of the frontline HCPs should be closely examined.¹⁶ In our study we have reported self-perceived levels of stress, resilience and moral distress among the HCPs. In this survey, the participants reported increased levels of stress, lower levels of resilience and high levels of moral distress. All of these findings correlate with each other. This means that higher levels of stress are associated with lower levels of resilience and higher levels of moral distress. The findings of our study are consistent with the previously mentioned studies.

It was interesting to note that more participants feared transmitting the infection to others rather than getting themselves infected. This may be due to the fact that people tend to show pro-social behavior under stressful conditions.¹⁷

There are certain limitations to this study. First one is the small sample size. Another one is the biased sampling that involves most participants between the ages of 20 and 30 years. Thirdly, the online data collection technique in itself has many flaws including generalized responses.¹⁸

Conclusion

The mental and psychological effects of the current COVID-19 pandemic are widespread. The HCPs face these effects head on. In addition to providing PPE to them, proper steps should be taken to preserve the mental health of our HCPs. Right actions taken timely will result in the provision of better healthcare to our patients, which is the basic aim of a sound health system.

Conflict of Interest: None

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Authors Contribution

MAK,SY: Conceptionlization of Project
AL,USA: Data Collection
AL,SY: Literature Search
QAD,HF: Statistical Analysis
SY,MAK: Drafting, Revision
SY,MAK: Writing of Manuscript

Burnout in Postgraduate Trainees and Consultants working in Psychiatry Departments of Teaching Hospitals in Lahore, Pakistan

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Abstract

Objective: To gauge the prevalence of burnout among postgraduate trainees and consultants working in psychiatry department, Services Hospital Lahore, Pakistan.

Methods: 31 trainee and consultant psychiatrists in Services Hospital Lahore, Pakistan participated in this cross-sectional study. Abbreviated Maslach Burnout Inventory (aMBI) measured burnout. It consisted of 9 items, relating to emotional exhaustion, depersonalization and personal accomplishment. Each item is scored on a seven-point Likert scale. For Emotional Exhaustion and Depersonalization, higher scores predicted greater burnout; Personal Accomplishment demonstrated the opposite, hence its scores were inverted. Participants with moderate scores in 2 or more dimensions were identified as suffering from burnout syndrome. Data was analyzed by SPSS 25.0.

Result: Mean age of participants was 34.87 ± 8.06 years. 52% were female. 58% were consultants, with average experience of 7 years; 61% practiced in more than one place. 32.3% of participants had burnout syndrome. Emotional Exhaustion subscale showed the highest scores i.e. 7.06 ± 3.43 . 71% of participants demonstrated moderate or high burnout in this scale. Average Depersonalization score was 2.94 ± 2.42 , while that for Personal Accomplishment was 3.29 ± 2.25 .

Conclusion: A significant portion of the sample reported moderate and high level of emotional exhaustion. On the contrary, we found low levels of depersonalization in the sample. Most psychiatrists reported adequate levels of personal achievement. These results are reassuring because, despite the presence of emotional burnout, psychiatrists still have capacity to empathize and provide adequate patient care.

Key Words: burnout, psychiatry, trainees, consultants, Lahore, Pakistan

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Introduction

Burnout is defined as a syndrome comprising emotional exhaustion, depersonalization and reduced personal accomplishment.¹ It is often a side effect of medical training and practice, due to a myriad of stressors associated with clinical work. Stressors pertinent to psychiatry can include hostile patients, patient suicide and working with victims of violence. Psychiatrists who lose a patient to suicide

may be plagued by guilt.² Psychiatry as a specialty is emotionally taxing; empathy and maintaining objectivity while being emotionally available for patient can be draining. The chronicity of psychiatric conditions and delayed progress in patients can lead to feelings of helplessness and frustration.³

Consequences of burnout are faced by both the psychiatrist and the patient. As the clinician fails to cope, psychological manifestations of burnout emerge, including depression, anxiety and substance abuse.^{4,5} Suicidal ideation has also been reported by trainees.⁶ Rich and Pitts found psychiatrists to have twice the risk of committing suicide.⁷ Burnout may compromise the quality of care, increase the probability of mistakes, decrease performance, lead to a sense of inadequacy and cause a spillover of work-related stress in family life.⁸ Some doctors may, even if unwittingly, avoid particular patients or situations.² The psychological

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and work-related ramifications of burnout are alarming, and it poses a considerable threat to physician well-being.

Physician well-being has long been a neglected matter. Doctors are an essential pillar of the health care system. They put their duties before their mental and physical health, which suffer consequently. Burnout is an urgent issue which must be addressed. While previously research has been carried out to measure burnout in specialties like medicine, surgery and gynecology, we found a dearth of research relating to psychiatric trainees and consultants. In the present study we will gauge the prevalence of burnout in this population and attempt to bridge the prevailing gap in data.

Methods

A cross-sectional study was conducted over a period of one month, from 11 September to 11 October 2020. The participants were postgraduate trainees and consultants working in psychiatry department, Services Hospital Lahore, Pakistan. The sample size for this research was 31. Participants were chosen via convenience sampling and informed consent was obtained from each subject.

A structured questionnaire was utilized to record demographic characteristics and intensity of burnout. The self-reported questionnaire was administered via Google Forms, owing to the ongoing covid-19 pandemic. The demographic characteristics are shown in Table 1. Burnout was measured by the Abbreviated Maslach Burnout Inventory (aMBI), as shown in Table 3. It is a valid and reliable measure.^{9,10} It measured three dimensions of burnout: emotional exhaustion, depersonalization and personal accomplishment. Abbreviated Maslach Burnout Inventory consisted of 9 items: questions 3, 4, 7 were related to emotional exhaustion; questions 2, 5, 8 were related to depersonalization; questions 1, 6, 9 were related to personal accomplishment. Each item was responded to on a Likert scale, ranging from “Never” (scored as 0) to “Everyday” (scored as 6). The score of each dimension ranged from 0-18. For the first 2 dimensions higher scores predicted greater burnout, while the third dimension demonstrated the opposite. Thus, the scores of personal achievement subscale were inverted so that higher scores reflected greater burnout, allowing for uniform interpretation of scores in all

three scales. The Abbreviated Maslach Burnout Inventory defines burnout as moderate scores in 2 or more dimensions. Data was entered into and analyzed by SPSS 25.0. For quantitative variables, mean and standard deviations were calculated. For qualitative variables, frequency and percentage distributions were generated.

Ethical approval was obtained from the institutional review board, RefNo. IRB/2020/692/SIMS.

Results

Thirty-one participants responded to the questionnaire over a period of one month. The demographic characteristics are shown in Table 1. The mean age of the participants was 34.87 ± 8.06 years. 52% of the respondents were female. 58% were working as consultants, with an average of approximately 7 years of experience; 61% of them practiced in more than one place. 46% of the psychiatric trainees were PG-2, while 30% were PG-3. The average scores of each subscale are shown in Table 2. Emotional exhaustion subscale showed the highest scores i.e. 7.06 ± 3.43 . 64% of the participants demonstrated moderate burnout in this scale. Low burnout was exhibited in the depersonalization scale by 90% and in the personal achievement scale by 74% of the participants. 10 (32%) participants demonstrated moderate burnout in at least 2 subscales, fulfilling the criterion for burnout as defined by Abbreviated Maslach Burnout Inventory.

Discussion

Table 1: Demographic Characteristics

Demographic Characteristics	Number	%
Age (years)	34.87 ± 8.06	-
Sex		
Male	15.00	48.39
Female	16.00	51.61
Working as:		
Trainee:	13.00	41.94
PG1	1.00	7.69
PG2	6.00	46.15
PG3	4.00	30.77
PG4	2.00	15.38
Consultant	18.00	58.06
Duration of Practice (years):	6.83 ± 5.83	
Do you practice in more than one place? (for consultants)		
Yes	11.00	61.11
No	7.00	38.89

Table 2: Average Scores and Frequency of Burnout in each Subscale

Scale	Average score (SD)	Low Burnout		Moderate Burnout		High Burnout	
		n	%	n	%	n	%
Emotional Exhaustion	7.06 ± 3.43	9	29.03	20	64.52	2	6.45
Depersonalization	2.94 ± 2.42	28	90.32	3	9.68	0	0
Personal Achievement (inverted scores)	3.29 ± 2.25	23	74.19	8	25.81	0	0

Table 3: Frequency of Responses to Individual Items of the aMBI by the Participants

Items	Every day		A few times a week		Once a week		A few times a month		Once a month or less		A few times a year		Never	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%
I deal very effectively with the problems of my patients	20	64.52	6	19.35	5	16.13	0	-	0	-	0	-	0	-
I feel I treat some patients as if they were impersonal objects	0	-	2	6.45	1	3.23	4	12.90	6	19.35	9	29.03	9	29.03
I feel emotionally drained from my work	0	-	7	22.58	1	3.23	9	29.03	5	16.13	8	25.81	1	3.23
I feel fatigued when I get up in the morning and have to face another day on the job	0	-	2	6.45	3	9.68	8	25.81	10	32.26	7	22.58	1	3.23
I've become more callous towards people since I took this job	0	-	0	-	3	9.68	0	-	5	16.13	11	35.48	12	38.71
I feel I'm positively influencing other people's lives through my work	12	38.71	8	25.81	5	16.13	6	19.35	0	-	0	-	0	-
Working with people all day is really a strain for me	0	-	2	6.45	2	6.45	10	32.26	2	6.45	10	32.26	5	16.13
I don't really care what happens to some patients	0	-	0	-	0	-	0	-	3	9.68	5	16.13	23	74.19
I feel exhilarated after working closely with my patients	7	22.50	11	35.48	6	19.35	3	9.68	2	6.45	2	6.45	0	-

According to our data, 32% of the psychiatrists suffered from burnout syndrome. The constant demand of emotional labour may put psychiatrists at risk, more so than other specialties. A Canadian study reported that 21% of the psychiatric residents experienced burnout.¹¹ Martini et al. found 40% of psychiatry trainees to be suffering from burnout.¹² An Irish study found 75% of child psychiatrists were struggling with burnout; however, since this study utilized the Copenhagen Burnout Inventory it is harder to draw comparisons.¹³

Our sample showed higher levels of burnout in the domain of emotional exhaustion: 71% had moderate or high burnout. This is slightly higher than the scores presented by Kumar et.al, where almost 67% experienced emotional exhaustion.¹⁴ Fülöp et al. found high emotional exhaustion among psychiatrists to be 32.8%.¹⁵ Emotional exhaustion can render the physician unable to emotionally connect with their patients, as their emotional resources are expended. To the

question “I feel I treat some patients as if they were impersonal objects”, 26% of the participants reported that they experienced this a few times a year, while 16% reportedly experienced this once a month or less. Almost 32% and 26% reported that the thought of going to work was draining, once month or less and a few times a month respectively. 32% of the respondents found working with people all day to be a strain a few times a month; a similar percentage reported to experience this once a month or less.

The depersonalized physician treats their patient with indifference. Our sample reported low levels of depersonalization; almost 10% were revealed to have moderate burnout in this scale and none reported high burnout. A study in New Zealand found that 26% and 13% of the psychiatrists had moderate and high burnout in this scale, respectively.¹⁴ Similarly, another research found 29.9% of the psychiatrists struggled with depersonalization.¹⁵ The questions “I don't really care what happens to some patients” and “I've become

more callous towards people since I took this job” were overwhelmingly dismissed by respondents in our sample. This shows that despite the high prevalence of emotional burnout, the clinicians are still capable of caring for, and about, the patient. However, we must treat these figures with cautious optimism.

Personal accomplishment scores were inverted, so that higher scores corresponded to greater burnout, similar to emotional exhaustion and depersonalization. It is reassuring that a majority of psychiatrists reported high levels of sense of achievement. Burnout In Consultants in Ireland Study (BICDIS) showed similar results regarding the dissonance among the Emotional Exhaustion and Personal Accomplishment scales.¹⁶ In our sample, 64% believed that they deal very effectively with the problems of their patients. Most psychiatrists felt that they have a positive impact on their patients’ lives.

Our study demonstrates optimistic findings regarding sense of accomplishment and empathy in psychiatrists. However, it is clear that physician wellbeing is an issue we must contend with in a timely manner, or we could be faced with dire consequences relating to physician health and patient care in future. Spickard suggests that physicians should be encouraged to take part in self-care activities, including spiritual activities and spending time with loved ones.¹⁷

This study used a self-reported measure which, although convenient, can introduce inaccuracies in the obtained data. However, we have used the Abbreviated Maslach Burnout Inventory as a tool to merely screen for the possibility of burnout and detect those at risk. Our results have been derived from a sample chosen by convenience sampling. This could impart some level of sampling bias to our results. Moreover, our limited sample size makes it difficult to make solid inferences. Our study does not attempt to find correlations between workplace and personal variables and burnout. Further research on burnout, consisting of a nationwide sample, focusing on variables associated with physician burnout is critical.

Conclusion

32% of the psychiatrists were afflicted by burnout syndrome in our sample. A significant portion reported moderate and high level of emotional exhaustion; on the contrary, we found low levels of depersonalization to be prevalent in the sample. Most psychiatrists

reported adequate levels of personal achievement. These results are reassuring because, despite the presence of emotional burnout, psychiatrists still have the capacity to empathize and provide adequate patient care.

Conflict of Interest: None

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Authors Contribution

BA: Conception & Initial Writing of Manuscript

RS, RM: Data Collection

RS, RM: Statistical Analysis

RS: Drafting, Revision

A Comparative Study to Assess the Efficacy of Streptokinase in Diabetic Versus Non-Diabetic Acute ST Elevation Myocardial Infarction Patients

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Abstract

Objective: Prominent resolution in the ST segment elevation on electrocardiogram(ECG), thrombolysis at the infarction site restoring perfusion determines the effectiveness of the streptokinase therapy. Hypercoagulable states and lack of efficacy with streptokinase is seen in diabetics. This study aimed to assess the thrombolytic efficacy of streptokinase in diabetic vs non-diabetics patients.

Methods: A cross-sectional study was conducted at Cardiology Department of Allama Iqbal Memorial Teaching Hospital, Sialkot from 1st September 2019 to 30th April, 2020. Total 504 patients of which 185 diabetics and 319 non-diabetic were selected. All the patients presenting with first episode of acute ST-elevation myocardial infarction were thrombolysed with 1.5million units of streptokinase within 12hours from the onset of their typical chest pain symptoms. A complete record of ECG changes was kept before and 90 min after thrombolysis with streptokinase. Chi-square test was applied and p value <0.05 was considered significant.

Results: 89.19% diabetic patients had >70% resolution of ST segment changes in comparison to 95.61% non-diabetics. 16.76% of the diabetic patients had increased ST-segment elevation post thrombolysis (P-value 0.001). 8.11% and 10.81% reinfarction rates during hospital stay and at one month post-thrombolysis were recorded in diabetics. Reduced left ventricle Ejection Fraction was seen in 62.16% and 58.62% of the diabetic and non-diabetic patients(P-value<0.005).

Conclusion: Comparatively decreased efficacy of streptokinase is seen in diabetic patients with reduced resolution of ST-segment. In correspondence with reduced left ventricle EF, re-infarction and stroke episodes.

Key Words: Streptokinase, acute myocardial infarction, STEMI, diabetes mellitus, hypercoagulability, atherosclerosis.

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Introduction

In Pakistan, one of the major cause of increasing mortality and morbidity is myocardial infarction

mainly due to atherosclerosis of the coronary arteries.¹ Acute myocardial infarction has mainly increased the death ratio in many world leading countries.² Majority of the population in Pakistan between 46-55 years of age are at risk of myocardial infarction.³

Diabetes mellitus is one of the main co-morbidities associated with myocardial infarction others being dyslipidemia, smoking, hypertension and previous episode of ischemic heart diseases.⁴ High blood sugar or glucose levels in diabetics identifying poor glyce-mic control are important cause of hypercoagulable states in diabetic patients.⁵ Therefore, hypercoagulable state risk is considered more common in diabetic population.⁶ Also fibrinolysis is decreased in diabetics

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as a result of increased plasminogen activator inhibitor type 1, thus progressive thrombus formation and accelerated plaque formation.⁷ This increases the incidence of myocardial infarction among diabetics as compared to non-diabetics. ST-segment resolution is a predictor to see the outcomes in myocardial infarction patients.⁸ Early thrombolysis with streptokinase in acute stage of myocardial infarction to restore blood supply of the myocardial cells is the main goal. Significant ST segment changes on ECG after thrombolytic therapy is more economical for accessing the prognosis of the disease, comparatively to coronary angiogram. Increased mortality and morbidity is observed widely in diabetic patients post thrombolysis.⁹

Our study mainly aimed at assessing the efficacy and outcomes in diabetic patients receiving thrombolytic therapy with streptokinase in acute myocardial infarction and comparing the results with non-diabetic patients. The efficacy of streptokinase associated with diabetic population will be assessed by electrical parameters (ECG changes) >70% or <70% ST-segment resolution, relieve of typical chest-pain symptoms, raised CK-MB levels, number of re-infarctions or stroke episodes and left ventricle ejection fraction (E.F%) estimation through echocardiography post-thrombolysis. This will help choose different treatment options as coronary interventions in diabetic patients with associated morbidities especially acute myocardial infarction.

Methods

A cross-sectional study was conducted at the department of cardiology, Allama Iqbal Memorial Teaching Hospital, Sialkot. The data was collected over a period of eight months from 1st September, 2019 till 30th April, 2020 through electronic databases. After informed consent, 504 patients were carefully registered of which 185 were diabetics and 319 non-diabetics. After confirmation their data (including their complete medical or any surgical history) was entered on the computerized database. The inclusion criteria had patients (diabetics or non-diabetics) with first episode of MI, suffering from typical chest-pain for >30mins but <12hours, ST-segment elevation in concordant leads on ECG and were thrombolysed with streptokinase within 12 hours from onset of their symptoms. Pregnant females, those patients with any

contraindications to thrombolysis with streptokinase, other than ST-segment ECG changes, with chest pain for >12hours, having previous cardiac intervention or history of ischemic heart disease were in the exclusion criteria. The patients were divided into two groups i.e diabetics and non-diabetics. Only previously diagnosed diabetic patients (HbA1C levels >6.5%) were enrolled. The study is approved by research and ethics committee of KMSMC/AIMTH, Sialkot letter No.46/REC/KMSMC Date:04/01/2020.

An ECG was obtained on presentation and 90 minutes after streptokinase therapy for complete record. The outcome of thrombolysis with streptokinase in both the groups was assessed based on electrical parameters, relieve of patient symptoms, tachycardia episodes, reduction in left ventricle systolic function by calculating EF(%) on bedside echocardiography and post thrombolysis reinfarction or stroke episodes. The electrical parameters were assessed whether the patient had increased or persistent ST segment elevation, or had >70% decrease / resolution in ST segment elevation after administration of streptokinase, which is considered to be a successful reperfusion sign. ECG reporting was done by a single senior E.R doctor to avoid any discrepancies in interpretation. Similarly, continuous monitoring for any re-infarction (with raised Ck-MB levels or new concordant ST-segment elevations on ECG within 6 days of patients hospital stay) was done. Episodes of cerebrovascular accidents of the same patients were recorded easily due to re-admission of the patients to the same hospital. Regular follow-ups of all the enrolled patients were ensured every 1 month for first six months after their acute MI episode by repeated telephonic reminders and than updating their data on electronic data collection devices respectively.

The data were analyzed by using SPSS version 23. Mean and standard deviation were used to calculate quantitative variables as age. Both (male & female) genders were included as qualitative variables and were measured using percentages. Outcome variables for successful reperfusion were recorded and the results compared between diabetics and non-diabetics groups using Chi-square test. P-value of <0.05 was considered significant.

Results

A total of 504 patients were enrolled, of which 185

were diabetics and 319 non-diabetics, mean age in the diabetic group was 54±9.6yrs as compared to 57±13.3yrs in non-diabetics (table 1). Age range was between 44 to 64yrs in diabetics and 42 to 71yrs in the non-diabetic group. Among the diabetic group 90 (48.65%) were males and 95 (51.35%) were females whereas, the other comparative group of non-diabetics had greater number of males 232(72.72%) than 87 (27.27%) females with the significant P-value of 0.001. Average basal metabolic index (BMI) of 33.71±9 was calculated in diabetic population and 23.51±7.5 in non-diabetic group. According to the

Table 1: Baseline Characteristics of Patients

	Diabetics	Non-diabetics	p-value
AGE	54±9.6 (34.3%)	57±13.3(65.7%)	.082
GENDER			
Male	90 (48.65%)	232 (72.72%)	.001
Female	95 (51.35%)	87 (27.27%)	
BMI	33.71±9 (37.8%)	23.51±7.5(62.2%)	.603
Cholesterol	185.19±37.52 (35.0%)	170.81±38.34 (65.0%)	.037
HbA1c	9.65±2.66 (46.4%)	6.01±0.76 (53.6%)	.008

Table 2: Post Streptokinase Therapy Efficacy Determinants

	Diabetics		Non-Diabetics		P-Value
	count	%	count	%	
Symptoms relieved	98	52.97%	258	80.88%	.004
Inhospital rethrombolysis	15	8.11%	10	3.13%	.000
One month reinfarction	20	10.81%	15	4.70%	.004
One month stroke	3	5.0%	0	0.0%	.041
Six month reinfection	5	2.70%	0	0.0%	.280
Six month stroke	2	1.08%	0	0.0%	.447
St-Segment Elevation increased	31	16.76%	0	0.0%	
St-Segment Resolution >70%	165	89.19%	305	95.61%	.001
St-segment Resolution <70%	20	10.81%	14	4.39%	
CK-MB (raised)	8	4.32%	7	2.19%	0.063
Heart rate >100 bpm	80	43.24%	105	32.92%	0.013
Reduced LV ejection fraction	115	62.16%	187	58.62%	0.000

biochemical parameters significantly increased HbA1c values 9.65±2.66 were seen in the diabetics with P-value 0.008. Blood cholesterol levels were found deranged among the two groups. (table 1)

52.97% of the diabetics and 80.88% non-diabetics had their symptoms relieved with a significant P-value 0.004 (table.2). The incidence of re-infarction in diabetics during their hospital stay (<6 days) was 8.11% (P-value 0.000) and 10.81%(P-value .004) after one month. With regards to the electrical activity our results showed that 16.76% (P-value 0.001) of diabetics showed increased or persistent ST segment elevation. 95.61% of the non-diabetics in comparison to diabetics 89.19% had >70% reduction in the ST-segment post thrombolysis(P-value 0.001). About 10.81% diabetics in group 1 had <70% ST segment resolution after thrombolytic therapy. 43.24% diabetics had episodes of tachycardia (H.R >100bpm) and 62.16%(p value <0.005) had reduced left ventricular ejection fraction in comparison to 58.62% non-diabetic MI patients(table 2).

Discussion

Thrombolysis with streptokinase is an effective and well known treatment option in patients presenting with acute ST-elevation myocardial infarction. Presence of associated co-morbidities or late (>12hours) presentation can affect the efficacy of streptokinase therapy¹⁰. All the patients in our study presented in >30mis from the onset of their symptoms but not more than 12 hours. Diabetes is one of the main risk factors associated with cardiovascular diseases.¹¹ Increased morbidity is associated with diabetic acute MI patients and reduce effect of streptokinase was seen in a research by varshit hathi.¹² This led us to make a hypothesis that diabetes solely may effect the efficacy and the outcomes of streptokinase therapy. Therefore, we conducted this study to assess the efficacy of streptokinase and compared the results specifically among diabetic and non-diabetic groups with acute ST-elevation myocardial infarction.

The mean HbA1c levels in diabetic population were 9.65±2.66 and 6.01±0.76 in non-diabetic group. HbA1c is one of the important biomarkers to diagnose diabetes and to monitor its prognosis.¹³ Therefore, HbA1c is used as continuous risk measurement variable for coronary artery diseases. Post thrombolysis reduced or decreased ST-segment resolution is seen significantly in diabetic patients in comparison to non-diabetics.¹⁴ This was quite similar to our study results where comparatively reduced ST-segment resolution was seen in the diabetic group, 10.81% of the diabetics had <70% resolution of ST-segment and 16.76%

showed persistently increased ST-segment elevations post thrombolysis (P-value 0.001). Significant resolution of ST-segment was seen in 95.61% non-diabetic group (P-value 0.001) with no persistent or increase elevations post thrombolysis.

Among diabetic patients 98(52.97%) had their typical chest pain symptoms relieved after thrombolysis with streptokinase whereas 258 out of 319 non-diabetics patients had their typical chest pain symptoms relieved with a significant p-value (0.004). 8.11% of the diabetics had re-infarction during their hospital stay and were re-thrombolysed with streptokinase in comparison to only 3.13% non-diabetics. According to our results the risk of stroke at one month in diabetics was 5% and 1.08% at six months with no episodes seen in the other comparative group. So was the risk of six month re-infarction which was common in diabetics. These results were consistent with the Framingham heart study, which proved after 20 years of trials that diabetic patients have two-fold to three-fold increased risk of clinical atherosclerosis and the cardiovascular disease mortality was greater for diabetic women as compared to diabetic men but after adjustment of other associated risk factors it was same for men and women.¹⁵

Similarly, other determinants as heart rate and effect on left ventricle ejection fraction after streptokinase therapy were assessed. Some researchers stated that patients with diabetes respond poorly after thrombolytic therapy.¹⁶ As was seen in our study results 43.24% diabetics had episodes of tachycardia (heart rate >100bpm) and most of them 62.16% had reduction in their left ventricle ejection fraction in comparison to 58.62% non diabetic patients. The limitations to our study included that we collected data from only one center with patients belonging to same ethnic backgrounds. Moreover, poor compliance of patients with medication and sedentary life styles were noticed. Therefore, more attention is required for treating diabetic myocardial infarction patients. Other treatment options as coronary interventions may be considered in diabetic acute STEMI patients.

Conclusion

In comparison to non-diabetics, decrease efficacy of streptokinase is seen in diabetic patients with reduced resolution of ST-segment. Post thrombolysis failure was correlated with reduced EF, re-infarction and stroke episodes.

Conflict of Interest: None

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Authors Contribution

HZ: Conceptionlization of Project

RB: Data Collection

RN: Literature Search

IA,RN,CJI: Statistical Analysis

RN: Drafting, Revision

RN: Writing of Manuscript

Determinants of Diagnostic and Treatment Delay Among Thalassemia Patients in Sialkot

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Abstract

Objectives: To find out determinants of diagnostic and treatment delay among patients with thalassemia major in Sialkot.

Methods: A cross-sectional analytical study was conducted in Sundas Foundation, Sialkot, from April 2019 to July 2019. A total of 120 patients were selected by convenient sampling and data was collected through semi-structured, pre-tested questionnaire. Important determinants considered were age, gender, literacy of parents, previous knowledge of disease and first health care facility visited. Data was analysed on SPSS version 25.0 and presented in the form of tables and figures. Chi-Square test was applied to study relationships between diagnostic and treatment delays with sociodemographic profile and other factors. P-value < 0.05 considered significant.

Results: There was considerable delay of 30-180 days in diagnosis of thalassemia patients (37.5%), 42.7% patients diagnosed in less than 30 days. Treatment delay of 7-21 days in 18% patients seen, 71% started treatment within a week. 30-180 days delay in seeking medical care, was observed in 20.8% patients. Only 24.2% patients visited government health facility for medical care. First facility visited and delay in seeking medical care were significantly associated with diagnostic delay (p value 0.000 and 0.005 respectively). Only 16.7% had previous knowledge about thalassemia and 21.6% parents knew about legislation regarding mandatory pre-marital screening for thalassemia.

Conclusion: Among important determinants, first health care facility visited and delay in seeking medical care had significant relationship with diagnostic delay. Better accessibility to healthcare facilities can overcome them.

Key words: Diagnostic Delay, Treatment Delay, Thalassemia, Determinants

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Introduction

Thalassemia is an important public health challenge in both developed and developing countries

with an estimated number of 330,000 affected newborns annually.^{1,2} About 3% of the world population carries genes for beta thalassemia and it is estimated that every year about 60,000 thalassemia babies are born all over the world³ and 270 million people are carriers of hemoglobinopathies. Approximately 79% of affected births are in the Asian population. Beta thalassemia is most prevalent in South China, Mediterranean, Arab countries, South East Asia, Africa and Iran with reported ranges from 2-25%.⁴ In Pakistan, the prevalence of thalassemia is 6-7% and is present in all ethnic groups. Carrier rate is 5-8% and there are about 9.8 million carriers in total population with around 6000 children diagnosed with beta thalassemia in Pakistan each year⁵ where 5% of population has thalassemia minor and disease burden

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estimated to range between 50,000-100,000 patients, which is 5% of patients globally.⁶ There were 25,000 children registered with Thalassaemia Federation of Pakistan in 2016. However, the actual figure is much higher as 1 lac of the rural population is not registered with Thalassaemia Centers.⁷

Only one similar was conducted previously regarding the factors that affect the delay in diagnosis, however, it takes into account all haemoglobinopathies. It was a cross-sectional study conducted in Iran in 2015, where 1002 enrolled patients were taken into account. The diagnostic delay was observed among 64.9% of the patients with a mean of 13.4 months.⁸

This study takes into account two types of delays i.e. diagnostic delay and treatment delay that ultimately contribute to a total delay. Total delay is the time interval from the onset of the illness until the initiation of treatment. Diagnostic delay is defined as the time interval between the onset of symptoms and labeling of the patient as diseased. It may be due to parent's delay in bringing the child to health care or physician's delay in diagnosing the disease, whereas treatment delay is defined as the time interval between disease diagnosis and disease treatment.⁸ Delay is important to study in thalassaemia as any sort of delay in diagnosis and treatment would result in worsening of prognosis and decreased survival rate. It is also associated with increased complications requiring advanced treatment and increase in morbidity and mortality. Not long ago, children born with thalassaemia seldom survived after their first decade of life but nowadays the survival of patients with beta thalassaemia major is increasing because of better treatment and supportive measures.⁸

The objective was to study the diagnostic and treatment delay among thalassaemia patients in Sialkot and its determinants.

Methods

It is analytical cross-sectional survey conducted during April to July 2019 at Sundas Foundation, Sialkot, which is a non-government organization providing blood transfusion to registered patients of Thalassaemia, Leukaemia and Haemophilia. From amongst the patients suffering from Thalassaemia, a sample size of 120 patients taken for this study through convenience sampling, based on feasibility and available resources of the study. A semi-structured questionnaire used for

data collection. All male and female patients below or equal to 25 years accompanied by any parent or family member, diagnosed with thalassaemia and willing to participate were included. Before data collection, a pre-tested, semi-structured questionnaire devised and translated in local language. A training session for interviewers conducted in effort to conduct the interviews in same tone and duration so that intra-observer bias minimized. A formal permission obtained from the institution and organization. Before starting the interview, patients and parents of patients informed about the objective of study, verbal informed consent taken, and parents assured about the confidentiality of information. The foundation visited during the 6 working days of the week and on average, 8-10 questionnaires were filled daily. Patients' names noted in a separate list and assigned serial numbers, and it made sure that same patients were excluded upon each visit. Upon data entry, only serial numbers used for identification of subjects.

Some of determinants related to delay in thalassaemia diagnosis and treatment included: socio-demographic profile including gender, age, type of residence, parental education and income. Patient related determinants such as knowledge, preferences to the type of health facility were included. Similarly, health system related determinants such as accessibility of health facility, counselling of the parents about thalassaemia prevention and treatment, number of visits, first contact with health professional and expertise of health care personnel. The frequency of these characteristics calculated by descriptive analysis. Delay was noted on the basis of Healthcare system delay – which included both delay in seeking medical care (the time patients took in seeking healthcare) and diagnostic delay (the time taken by physicians to diagnose the illness), and Treatment delay (the time that was taken in starting the recommended treatment). The collected data was analyzed on SPSS Version 25.0 and presented in the form of tables and figures. The relationship between diagnostic/ treatment delays and age, gender, education of father, education of mother, income of father, type of living, frequency of visit, previous knowledge about thalassaemia program and knowledge about legislation was analyzed by cross-tabulation and Chi-Square test was used as a test of significance with P value < 0.05 as significant.

All ethical considerations ensured at every step. Anonymity and autonomy of the participants was

taken care along with confidentiality of data. An informed consent was taken from the parent/guardian in case of minors (age less than 15 years).

Results

The socio-demographic characteristics of the patients and their parents in Sialkot shown in Table 1. Among 120 patients, with mean and median age 9.741 +4.77 SD and 13.5 respectively, 54.2% were male patients, 57.7% lived in rural areas. The fathers of 56.7% patient and mothers of 57.5% patients received formal education. The fathers mean income was 16,166.67 +1000.6 SD and median income of 15,000 showing that 48.3% fathers were having income less than 15000 rupees.

For the determinants of delay, Table-2 shows that out of 120 patients, 75.8% people preferred to visit a

Table 1: Descriptive Statistics of Thalassemia Patients According to their Socio-Demographic Profile (n=120)

Characteristics	Frequency	Percentage (%)
Age (Years)		
Less than 5	24	20.0%
5-9	43	35.8%
10-15	40	33.3%
Above 15	13	10.8%
Gender		
Male	65	54.2%
Female	55	45.8%
Type of Living		
Urban	51	42.5%
Rural	69	57.5%
Education of Father		
Formal education	68	56.7%
No formal education	52	43.3%
Income of Father (Pakistani Rupees)		
<15,000	58	48.3%
15-20,000	25	20.8%
>20,000	37	30.8%
Education of Mother		
Formal education	69	57.5%
No formal education	51	42.5%

private health facility, being accessible was the most common reason of visit for 43.3% people. Out of 120 patients 62 (51.67%) visited fortnightly. Regarding knowledge, 83.33% did not have any previous knowledge about thalassemia, 65.83% mothers did not receive any counselling in the subsequent pregnancies,

76.67% were having no knowledge about the national thalassemia prevention program, and 78.33% were unaware of any legislation regarding thalassemia in Pakistan. Only 42/120 (35%) had history of thalassemia in their family. Table 2 also shows association between different determinants and diagnostic and treatment delay was calculated by applying chi square test (P < 0.05 taken as significant). All determinants under study had insignificant association with diagnostic delay except the first health care facility visited

Table 2: Descriptive Statistics of Thalassemia Patients According to Determinants of Delay (n=120)

Determinants	Frequency	Percentage (%)	P-value Diagnostic Delay ¹ Treatment Delay ²
First health facility visited for seeking medical care			
Private	91	75.83%	0.0001*
Govt. hospital	27	22.50%	0.9012
Hakeem	02	1.67%	
Reason for consultation with health facility			
Accessible	52	43.30%	0.1041
Confidence in treatment	43	35.80%	0.5872
Referred	25	20.80%	
Frequency of visits to the health facility			
Weekly	38	31.67%	0.7091
Fortnightly	62	51.67%	0.6472
Monthly	20	16.67%	
Previous knowledge about thalassemia			
Yes	20	16.67%	0.6741
No	100	83.33%	0.9292
Family history of thalassemia			
Yes	42	35%	0.7811
No	78	65%	0.7422
Counselling for subsequent pregnancy			
Yes	41	34.17%	0.9041
No	79	65.83%	0.7692
Knowledge about National Thalassemia Prevention Program			
Yes	28	23.33%	0.5751
No	92	76.67%	0.7142
Knowledge about legislations regarding thalassemia			
Yes	26	21.67%	0.8021
No	94	78.33%	0.3182
Delay in seeking medical care			
Less than 30 days	89	74.2%	0.0051*
30days and above	25	24.8%	0.2152

*p-value is significant (<0.05)

and delay in seeking medical care diagnostic delay (p value 0.000 and 0.005 respectively).

Taking into account the types of medical delays among Thalassemia patients (TP), Figure 1 shows that 20.8% patients encountered delay in seeking medical care extending from 30-180 days whereas 5% TP delayed seeking care from 181 days to 365 days. The diagnostics delay of 30-180 days was found in 37.5% patients, whereas 14.3% patients had 181-365 days delay and 5.50% had delay in diagnostics for more than 365 days. Only 11% patients delayed their treatment for more than 21 days, 89% patients acquired medical treatment within 3 weeks.

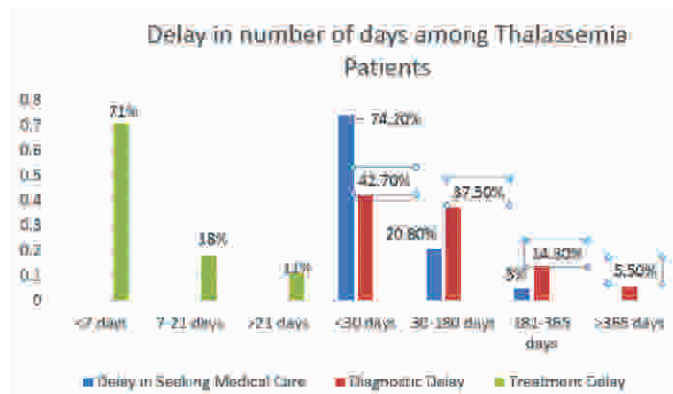


Fig 1: Delay in Number of Days Among Thalassemia Patients (n=120).

Discussion

The following study was conducted to study the diagnostic and treatment delays and its determinants among thalassemia patients (TP) in Sialkot. It showed that 51.8% patients had diagnostic delay from 1-12 month and 5.5% patients had delay above one year, 29% had treatment delay more than 7 days and 25.8% delayed seeking medical care. A retrospective study conducted in Iran with the objective of determining diagnostic delay in 1002 thalassemia patients, showed that 64.0% of the patients had diagnostic delay, most of them lying in the category of less than 12 months (44.1%).⁸ Wu et al argued that time of diagnosis is crucial for the treatment, complications and survival of the patients. Hassanzadeh et al showed that diagnostic delay in 65.3% of patients was significantly associated with their survival, arguing 25% of deaths could be avoided if delay in diagnosis didn't occur.^{9,10} Biswas J and her colleagues argued that treatment delayed is treatment denied with consistent relationship of delayed treatment with poor outcomes,¹¹

emphasizing the role of treatment delays among patients with chronic ailment. Caocci et al showed that despite the median diagnosis of TP at 8 months, the treatment started at median age of 11 months. Similarly, Mevada showed that delay in diagnosis and start of chelation therapy among TP had negative impact on their quality of life, adding mental health issues and social challenges.^{12,13}

In this analytical cross-sectional study having primary data with 120 sample size, two third of the patients were below 15 years with mean age being 9.741 years + 4.77; 54.2% being males and most of them from the rural background, and 48.3% belonged to families with income less than 15,000 PKR/month. The sociodemographic profile of this study is comparable with the TP enrolled in study Thailand and Bangladesh^{14,15} except that in a study of Bangladesh where 54.3% of their patients were below 5 years with mean age being 6years+3.66^{14,15} and 31.4% patients were from the lower income group.¹⁴ Like other studies, in this study, there was male predominance indicating gender disparity similar to other studies.^{8,14,15,16} Out of 120 patients, 10.8% patients were above 15 years. The number of <15 years patients is more than above mentioned studies where hardly any patient was < 15 years. Malik et al found that almost 38% of patients were above 15 years arguing that increasing mean age of TP means better survival among thalassemia families in last few decades.¹⁶ Moon et al also showed no such disparity, may be because the socio-cultural set up in modern Korea is different from South Asia.¹⁷ Malik showed that prevention and adherence to treatment affected indirectly by educational level of parent. Out of 120 patients, 68(56.7%) fathers were educated and 57.5% of mothers were educated. The literacy levels in the parents is slightly better than Iranian study but less than Malik's study where 65.2% fathers and 58% mothers had more than primary education.¹⁸

Studying the association of first visit to health facilities with diagnostic and treatment delay shows that this variable is statistically significant to diagnostic delay with p value 0.000. 75.8% of TP visited private clinic with most common reason was accessibility (43.3%) and confidence in treatment (35.8%). Zeydi et al identified that among others, accessibility is one of the barriers in among TP towards treatment while trust and friendly interaction with health care provi-

ders facilitated adherence it.¹⁸

Among 120 patients, treatment delay of less than 7 days showed in 71%. No other study on treatment delay among TP is published. The frequency of visit to the health facility was also calculated. 31.7% of the sample visited weekly while 51.7% visited fortnightly. About 16.7% of people visited the health facility on a monthly basis for blood transfusions. TP require at-least one dose of transfusion every fortnightly and up to five doses of iron chelation therapy per week, if needed. Thus, visits to the health facility indirectly indication the regularity and compliance to treatment along with the severity. Similarly, delay in seeking medical care related significantly to delay in diagnosis. Studies show that regular transfusions increase the survival of TP but delay in the onset of complication could lead to discontinuation of the therapy.^{19,20,21,22} Caocci et al showed different results where only 22% of the children had regular transfusion support and 78% of the patients had received irregular iron chelation therapy (less than once a week), reducing their health care facility visits for treatment sake.¹⁶

It is a well-established notion that effectiveness of prevention program especially for thalassemia requires health education, mass screening of the high risk, genetic counseling, prenatal diagnosis and legislation.^{16,23} This study showed that 23.3% parents had knowledge about thalassemia prevention program and 83.3% had no previous knowledge, 21.7% people had knowledge about legislation regarding thalassemia. Malik et al and Ishaq et al showed contrasting results where 68.9% and 44.6% of parents had knowledge about thalassemia but Ghafoor et al showed that only 15% of parents were aware of thalassemia previously. High knowledge in the previous two studies could be due to study settings as all these studies conducted in the tertiary hospitals and had large sample sizes. Only 34.1% parents received counselling for subsequent pregnancy in contrast to Malik et al where 64.5% parents received counselling.^{16, 23,24} This shows the lack of preventive and management tiers of the programme. Although Pakistan has adopted regulatory approach towards thalassemia for pre-marital screening in 2017,²⁵ only 21.6% of parents were aware of such efforts. However, Ishaq et al already showed that 87.9% of parents supported such legislation in 2009. It should be kept in mind that

in that study, 76.5% and 84.3% parents were aware of pre-marital screening and prenatal diagnosis respectively and the study was conducted in a leading Thalassemia Centre of the provincial capital.

The study under discussion is the first study conducted on the topic of diagnostic and treatment delays in patients of thalassemia in Sialkot. It was an attempt to cover all possible determinants of diagnostic delay and treatment delay in thalassemia patients. Face to face interviews were held, and primary data was collected (not secondary which is collected from the previous records of patients). But this study was not without limitations.

Major limitations were small sample size of 120 patients, selected by convenient sampling, using data of patients from single health facility for blood transfusion and resource constraints including time. Inability to cover older patients and other haemoglobinopathies was another limitation. Cohort Study design and subsequent follow up was not feasible. Moreover, Sialkot is just at a distance of two-hour drive from Lahore and people prefer utilizing health facilities of Lahore over Sialkot's. Future multi-centre studies on the same subject with a large sample size, can give better picture of the situation in the country. Efforts are required to increase awareness at different strata of public and health care providers so to prevent delay in both diagnosis and treatment.

Conclusion

In conclusion, the following analytical cross-sectional study is an attempt to determine delays in diagnosis and treatment among thalassemia patients in Sialkot, Pakistan. It was found that 1-12 months were taken by a quarter of thalassemia patients to seek medical care, 51.8% had diagnostic delay from 1-12 months and in 5.5% patients, it extended beyond 1 year. The treatment delay was >7 days for 29% of the patients. Among important determinants considered for their possible role, no relationship of delay found with socio-demographic profile. Delay in seeking medical care and type of facility visited was related to diagnostic delay. Hurdles like inaccessibility, lack of knowledge about thalassemia and its prevention can only be overcome by vigilant multi-pronged approach that incorporates both patient and health system related delays.

Conflict of Interest: None

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ZT: Conceptionlization of Project

PA: Data Collection

TF: Literature Search

MS: Statistical Analysis

KA: Drafting, Revision

MN: Writing of Manuscript

Variation of Body Mass Index and Peak Expiratory Flow Rate among Medical Students of CMH Lahore Medical College

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Abstract

Objective: To find out the variation of body mass index and peak expiratory flow rate among medical students of Combined Military Hospital, Lahore Medical College, Lahore, Pakistan.

Methods: A Cross-sectional study was conducted by undergraduate students of CMH, at CMH Lahore Medical College and Institute of Dentistry in September 2019 after Ethical approval from the Ethical Review Committee of the same institution. There were 138 1st year medical students. Demographic profiles of all the students were taken and height, weight, BMI, PEFR were measured. Participants were classified on the basis of their BMI values. Underweight (BMI<18.5), normal weight (18.5≤BMI≤24.9), overweight (25≤BMI≤29.9), and obese (BMI≥30). Correlational tests were applied to find out any statistically significant correlations. A p value less than 0.05 was considered significant.

Results: The mean BMI in females was 23.16±6.01 corresponding with that of mean PEFR value 325.23±62.30 whereas in males the mean BMI was 22.65±3.11 corresponding with that of mean PEFR value 433.97±101.84. There is a statistically significant variation in PEFR with gender (r=0.540, p=0.001) which can be explained on ethnic backgrounds. Males had a higher PEFR than females. However, there was no significant correlation between BMI and PEFR. Also, gender was not related to BMI.

Conclusion: In our study, PEFR is not affected by variation in BMI. However, gender is associated with PEFR. Males have a higher PEFR than females. This can be explained on the basis of ethnicity. BMI is not associated with gender. A large sample size with more accurate calculation of PEFR is needed for better evaluation.

Keywords: Obesity and lung function, PEFR and BMI, BMI and gender

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Introduction

Body Mass Index (BMI)- which is the measurement of weight relative to height- is the tool used worldwide to classify an individual as Overweight, Underweight or Obese. People having a BMI greater

than 25kg/m² are considered “Overweight” while those having greater than 30kg/m² are considered as “Obese”. Still, BMI is not a gold standard for the measure of degree of fatness in an individual.¹ An Emerging Global Health Peril is Obesity which has equally affected both developing and developed countries. Pakistan stands 165th /194 in the ranking of “World Fattest Countries” with 22.2% people crossing the subliminal level of Obesity.² Previous studies have shown a large number of medical students to be Overweight/Obese. Factors responsible for this include sedentary lifestyle, prolonged sitting, genetic influence, over-consumption of fast food, over-eating due to exam stress, and least physical activity.^{3,4}

Obesity- often referred to as mother of all diseases- puts a person to the peril of severe ailments including

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respiratory diseases.⁵ Increased fat levels decrease the lung compliance leading to various problems such as breathlessness and decreased exercise tolerance.⁶

Peak Expiratory Flow Rate (PEFR) is defined as the maximal flow of air that can be attained after maximum inhalation during a forceful exhalation. It is used as a tool to test the flow of air through the airway of a patient and to check for any obstruction in the lungs. The value of PEFR may vary with gender, age, race, and environment.⁷ Various studies have demarcated the Forced Expiratory Volume taken at the 1st second of forced exhalation (FEV1) to be a better indicator for airway obstruction than PEFR. Still, PEFR is preferable due to its portability, easy handling, patient feasibility and cost effectiveness. The Wright's Peak Flow Meter is commonly used in laboratories for PEFR measurement.⁸

This descriptive study aimed at assessing and documenting the BMI and PEFR of the newly enrolled medical undergraduates to describe the general health status of medical students. Previous studies^{7,9,10,13} indicate both positive and negative association of BMI with PEFR. We also aimed to re-check this correlation in our sample. Ethnic backgrounds and social factors are not considered in this study.

Methods

A cross sectional study was conducted by undergraduate students of CMH, at CMH Lahore Medical College and Institute of Dentistry in Sept. Ethical Approval was taken from Ethical Review Committee of CMH Lahore Medical College prior to the conduction of study. All the participants were assured that their identity will not be disclosed, and the data collected will be used only for research purposes. They were told that they could withdraw from the study any time if they have concerns. All their queries were addressed in details.

All students of 1st Year MBBS were included, the participants were between the ages of 17 and 22. The study variable were height, weight, BMI and PEFR. Protocols of the procedure were described clearly to all the students prior to the conduction experiment.

Vitals (blood pressure, pulse, respiratory rates) were measured for all the students prior to the measurement of PEFR. All the measurements were done with care under observation of the research team. Heights were measured in centimeters using stadiometer, and weights were measured using standard calibrated

weighing scales. PEFR was measured with Wright's Peak Flow Meter in Liter/minutes. Experiments were repeated thrice, and a mean was taken to reduce any error.

Demographic profiles of all the students, height, weight, BMI, and PEFR were recorded in the form of descriptive data. Pearson's correlation was applied to find out any significant correlations. P-value ≤ 0.05 was taken significant. Statistical Package for Social Sciences (SPSS v 25) was used for statistical analysis.

Results

Table 1 shows the distribution of study population. Male participants were larger in percentage and had a mean age of 18.93+1.045. Females had a mean age of 18.88+0.992.

Table 2. shows the variation of BMI with PEFR of the subjects. Table 3 and Table 4 provide a correlation of these values with gender. Only three out of 138 were

obese while 15 were underweight and 35 were overweight. A statistically significant correlation was found between PEFT and BMI in the underweight and normal-weight grouped people ($r=0.573$, $p=0.02$ in underweight people, and $r = 0.240$, $p = 0.02$ in normal-weight people). However, no significant correlation between BMI and PEFR was found in overweight and obese people.

The statistical analysis using Pearson's Correlation shows that there is no correlation between BMI and PEFR and also that gender is not related to BMI.

Table 2: Variation of PEFR with BMI

Relationship between PEFR and BMI			
BMI Range	Mean PEFR	N	Std. Deviation
Less than 18.5	389.33	15	77.318
18.5-24.9	380.00	85	103.003
25-29.9	388.00	35	110.155
30.0 and Above	366.67	3	28.868
Total	382.75	138	100.805

However, gender has a statistically significant correlation with PEFR.

Discussion

Obesity is an emerging problem in Pakistan, not least in women and young adults. This is due to sedentary

Table 3: Variation of BMI and PEFR with Gender

Gender, BMI and PEFR		
Gender	Mean BMI	Mean PEFR*
Male	22.65 \pm 3.110	433.97 \pm 101.84
Female	23.16 \pm 6.013	325.23 \pm 62.302

*Variation of PEFR with Gender ($r=0.540$, $p=0.001$)

lifestyles and unhealthy food habits. Our study demonstrates that PEFR in males was greater than in females. One explanation for this finding is based on height. A statistically significant relationship ($p<0.01$) is found between height and PEFR when studied for the combined data of both genders. In our study population, males were generally taller than females (the mean height of males was 173.28 \pm 6.67 cm and of the females was 158.62 \pm 7.93 cm). Given that (1) height is positively related to PEFR and (2) males are taller in this study population, this might account for the higher PEFR findings in males than females. Similar findings have been reported previously.¹⁶ An alternate explanation suggests that decreased PEFR in females might also be associated with decreased physical activity and ethnic background, but this is limited in its explanatory powers and was not tested in our work and thus cannot be objectively remarked upon without further study.

The results of our study are consistent with some of the studies done earlier and are in contrast with others. Our results show that there is no correlation between BMI and PEFR. This is in consistence with the study done by Harpreet⁷ and Saraswathi Ilango¹⁰ and in contrast with Sudha⁹ and Dharamshi.¹³ This contrast can be explained by the fact that the studies showing contrast results had a skewed sample i.e., increased population of either male or female gender.

Some studies¹⁰ hypothesize that body fat distribution might have effect on Lung functioning. Abdominal fat content might interfere with the mobilization of the diaphragm and thus decreasing lung functionality. They also hypothesize that lung function might be different in females and males because of different body fat distributions i.e., males have android obesity and females have gynecoid obesity. However, no significant experimental studies support this notion. Our study is also in contrast with this hypothesis. It indicates no correlation between BMI and PEFR.

In contrast to other studies,^{11,12} the BMI values were not found to be related with gender. Both males and females had almost an equal mean of BMI. The only significant correlation was that PEFR was higher in males than the females similar to other studies.^{12,13} This can be explained on the basis of ethnic and cultural differences. Ethnicity is considered as an important factor that affects PEFR.⁷ Most of the male participants of our study had a strenuous physical activity as a part of their daily routine. This might be a reason of marked differences in the PEFR values of males and females.

Limitations

A larger sample size with a detailed insight of ethnic background is needed to get more accurate results. Moreover, Wright's Peak Flow Meter is less accurate than its counterparts. This might put an error in the calculation of results. A more accurate Peak Flow Meter can be used to level up the accuracy of the acquired data.¹⁵

Conclusion

The study concludes that PEFR is not affected by variation in BMI. However, gender is associated with PEFR. Males have a higher PEFR than females. This can be explained on the basis of ethnicity. BMI is not associated with gender. A large sample size with more accurate calculation of PEFR is needed for better evaluation.

Conflict of Interest: None

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Authors Contribution

IF,IA,AKR: Conceptionlization of Project

BI,IA : Data Collection

AKR,MAS: Literature Search

HF,AKR: Statistical Analysis

IF,HF: Drafting, Revision

IF,IA: Writing of Manuscript

Evaluation of Protective Effect of Ajwa Seed And Fruit on Renal Histopathological Changes in Diabetic Nephropathic Rats

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Abstract

Objective: To investigate the protective effect of Ajwa date seed and fruit on renal histological changes in alloxan induced diabetic rats.

Methods: This was an experimental study and was conducted in Post Graduate Medical Institute. The duration of study was 6 weeks. In this study random allotment of 32 rats was done in four groups. Group 1 was treated as control. Diabetes was induced in the 2nd, 3rd and 4th group by alloxan injection intra peritoneally. Group 2 was diabetic non treated while group 3 and 4 were treated with Ajwa seed and flesh respectively. After six weeks, animals were anaesthetized and kidneys were then removed without delay and weighed. Kidney paraffin sections were prepared and stained with hematoxylin& eosin (H&E) and with Periodic acid Schiff (PAS) technique. Glomerular diameters were estimated. Glomerular volume determined by stage micrometer. Vascular, tubular injury and glomerular sclerosis were studied semi quantitatively.

Results: The data showed that Ajwa date seed significantly reduced hyperglycemia but did not normalize the fasting blood glucose. We found exceedingly significant improvement in kidney weight, glomerular diameter, tubular and vascular injury with Ajwa date seed suggesting reduction in diabetic nephropathy. Ajwa seed diet found more effective in reducing nephropathy than Ajwa fruit diet. Current study displayed that the seed of Ajwa showed significant improvement in renal histological characteristics in diabetic rats.

Conclusion: The findings showed that Ajwa date seed and flesh reduce loss of tubular and vascular damage in alloxan induced diabetes.

Key Words: Oxidative stress, Kidney, Diabetes, Ajwa, Antioxidant, histopathology

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Introduction

Diabetic nephropathy is the main cause of chronic kidney failure. The International Diabetic Federation stated a number of 440 million diabetics in the year 2015 which is anticipated to rise 550 million

by the year 2035. About 35% of diabetic patients observe renal disorders. Prolonged glycemia, race, sex, genetics and hypertension have been involved in the development of nephropathy in diabetes.¹ In Diabetic nephropathy, hyperfiltration progresses into macroalbuminuria and glomerular endothelial dysfunction leading to decrease in glomerular filtration rate and end stage kidney disease.²

Reactive oxygen species, inflammatory cytokines and growth factors are key players in this respect.³ Most of the studies reveal the implication of oxidative stress in diabetes pathogenesis by the alteration in different signaling pathways like renin angiotensin system, development of advanced glycation end products, lipid peroxidation, impaired glutathione metabolism and decreased levels of Vit C, lipids, glutathione peroxidase, catalase, superoxide dismutase, DNA damage are various indicators of oxidative

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stress in diabetes mellitus. Oxidative stress causes insulin resistance also.⁴ Hyperglycemia in kidney tissue induces mesangial expansion and causes changes in cellular and extra cellular glomerular structure, presented by glomerular basement membrane thickening, increased glomerular volume, diameter and glomerulosclerosis.⁵

Anti-diabetic drugs which are commonly used in the treatment of type 2 diabetes mellitus are sulfonylureas, biguanides, thiazolidinediones and α glucosidase inhibitors. None of these is devoid of adverse effects for example sulfonylureas carries risk of hypoglycemia, drug allergy and drug resistance when used for longer period of time. Biguanides can lead to diarrhea and lactic acidosis where as TZD carries risk of mild anemia and edema and may increase the risk of heart failure. *Phonex dactylefera* L. (Palmaceae) is grown mostly in Middle East and United States. Date fruit is used in diet as traditional medicine in many countries. Our previous studies have confirmed that date fruit and seeds have shown multiple bioactivities like antihyperglycemic⁷ and anti-nephropathic activities when given for 6 weeks to alloxanized rats because of having phytoelement like antioxidants, phenolics, flavonone, anthocynins. Previously published researches found the nephroprotective effects of *p dactylefera*.^{8,9} So considering the traditional use of date palm in the treatment of diabetes mellitus and in its complications, this study was carried out to investigate the protective effect of Ajwa date seed and fruit on histological alterations of kidneys in alloxan induced diabetic nephropathy.

Methods

Experimental study in Post Graduate Medical Institute Lahore for period of six weeks duration.

Ajwa collection and preparation of diet:

Two kilograms of Ajwa date was bought from Khajoor market Madina (Saudi Arabia). Department of botany - Govt. College Lahore identified and preserved specimen in herbarium after allotting voucher number (Herb.2954). The seeds were separated, washed, air dried and ground to form powder while fruit was cleaned and mashed finely. They were kept in air tight jars, labeling was done and stored in cool dry place for further use.

Animals

Thirty two Sprague dawley rats (healthy male) were

purchased from University of health sciences Lahore and divided into four groups (8 rats per group). They were kept in animal laboratory, Post graduate medical institute, Lahore. Controlled environmental temperature was sustained with 12 hr light and day cycle alternatively. Regular pallet diet mixed with rat chow and water was given ad libitum. Prior Approval of the current study was taken from ethical committee of Post graduate medical institute and advance board, university of health sciences, Lahore

Induction of experimental diabetes

Alloxan was freshly dissolved in normal saline just before use and given as a single intraperitoneal injection (150mg/kg) to fasting rats of all groups except normal control. After about 72 hours, animals showing blood glucose fasting level >250 and < 500 were chosen as diabetics and divided into four groups for study.

Dosage and treatment protocol:

Group I is normal control and normal saline single intraperitoneal injection was given. Rats from Group II, III and IV were given intraperitoneally, the alloxan monohydrate injection (150mg/kg). Group II was kept as diabetic control group. Ajwa seed powder (1.5 g) and Ajwa fruit (7g) were mixed to 100 gram of rat chow individually, small pallets were made and this diet was given to animals of group III & IV for six weeks continuously ad libitum after confirmation of diabetes. This every day diet requirement for rats was proposed on the basis of recommendations from Ahadith regarding the daily requirement for adult human being is seven dates.¹⁰

Determination of relative kidney weight and fasting blood glucose

Fasting blood glucose level was determined by the glucometer (Roche Accucheck performa).

Histological assessment of kidneys

After sacrificing rats, kidneys were taken out, weighed and fixed in buffered formalin (10% neutral). After fixation, tissue sections (5 μ m) were cut and embedded in paraffin wax.

Tissue sections were then stained with hematoxylin-eosin (H&E) and assessment of vascular and tubular injury was made under light microscope at 400X magnifications. Periodic Acid Schiff staining was

used to see the thickness of basement membranes of glomeruli, mesengial matrix and glomerulosclerosis¹¹. The slides were analyzed blindly by pathologist who designated the vascular, tubular injury, thickening of basement membrane and matrix on the scale: 0, absent; 1, negligible; 2, moderate; 3, severe.

Semi quantitative range was applied to study glomerulosclerosis, where 0 designated normal glomeruli, 1 designated sclerosis equal to 25% of glomeruli, and 2 equal to 25-50%, 3 equal to 50-75% and 4 equal to sclerosis in more than 75% of glomeruli.¹²

Glomerular diameters were measured by selecting randomly about 50-60 glomeruli in each kidney by stage method using oculomicrometer. Calibration value was calculated for one division of oculomicrometer. Two measurements, one cross wise and other right angle to it were measured and its mean was taken for diameter of one glomerulus.¹³

Statistical Analysis:

Histological parameters were presented with percentages. ANOVA (Kruskal Wallis) was applied to study the significance of effects in all study groups. Pair wise assessment and comparison of histopathological variables between groups was made by Mann Whitney U test.

Results

Treatment with Ajwa seed nearly normalized relative kidney weight and glomerular diameter

Relative kidneys weights were found highly significantly elevated (p 0.001) in diseased group when compared to control rats. Treatment with Ajwa seed highly significantly (0.01) lowered the relative kidney weights with comparison to diabetic rats. Effect of Ajwa fruit was not significant.

Glomerular diameters were found significantly increased (p 0.001) in diabetic group. Treatment with Ajwa seed highly significantly (p0.001) restored the glomerular diameter as compared to diabetic group. Ameliorative effect of Ajwa fruit was not significant (Table 1).

Treatment with Ajwa seeds and fruit alleviated histopathological injuries in diabetic rats

Examination of kidney histopathology revealed normal kidney histology in the control group (figure 1a). The untreated diabetic kidneys, compared to control group showed marked vascular, tubular injury and glomerulosclerosis in more than 50-70% of glomeruli (Fig 1b). Glomerular capillaries were irregular, widened and attached to bowman's capsule. Tubointerstitial damage was severe. There were only few widened tubules with early atrophy of epithelial cells. Moderate interstitial fibrosis was also observed. There was thickening of basement membranes and mesengial matrix as well as increase in the number of mesengial cells.

Treatment with Ajwa seed highly significantly alleviated tubular injury, improved the thickening of basement membrane, mesengial matrix and glomerulosclerosis (all p 0.01) and vascular injuries (p 0.001) compared with untreated diabetic group (Fig 1c). Similarly Ajwa fruit treated group also showed significant improvement in all of above histological injuries (all p0.05). Ajwa fruit treatment alleviated glomerulosclerosis but effect was not significant when compared to diseased group.

Discussion

P. dactylefera fruit and seeds have been consumed in folk medicine since long ago for treatment of diabetes mellitus. Few studies have demonstrated their antidiabetic effects but a lesser amount of data has been available to see the effect of seeds and fruit of dates on diabetic complications like nephropathy. The current study was carried out to probe the effects of Ajwa seed and fruit on nephropathy and histopathological changes of diabetic kidneys.

Most severe complication of diabetes is nephropathy and researchers have reported that progressive protein urea causes gradual declining of kidney function parameters which is the major risk factor for progre-

Table 1: Relative Kidney Weights & Glomerular Diameters

Parameter	Control	Diabetic	Diabetics on Ajwa seed diet	Diabetics on Ajwa fruit diet
Relative kidney weight(g/100g body weight)	0.413±0.025	0.581±.073###	0.46±0.74**	0.55±0.07
Glomerular diameter	96.2±0.6	121.5±6.0###	105.4±8.4***	112.1±9.7

Table 1: Treatment with both Ajwa seed and fruit almost normalized relative kidney weight and glomerular diameter. Data is shown as Mean±SD. n=8. ** and ***numerical difference as compared to diabetic group at p<0.01 and p<0.001 respectively. ## and ### numerical difference as compared to control group at p<0.01 and p<0.001 respectively

ssive renal impairment. Diabetic nephropathy is also related with increase in relative kidney weight, glomerular diameter, tubular damage, vascular injury and glomerulosclerosis.³

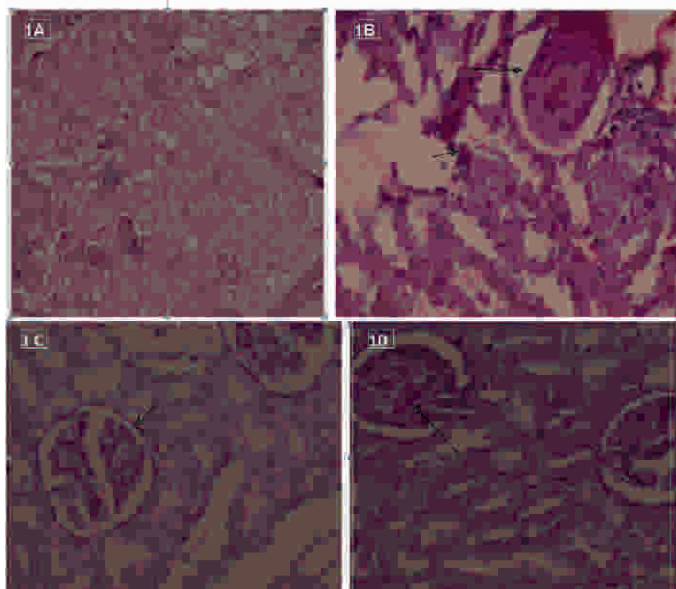


Fig 1: *Histopathological Changes in Kidneys of Control and Experimental rats. (1A- Group I) Normal Kidneys with Normal Glomeruli & Tubules - H&E 100X. (1B-Group II) Diabetic Kidneys Showing Severe Angiopathy, Thickening of Basement Membrane and Diffusely Moderate Glomerulosclerosis - PAS 400X. (1C-Group III) Ajwa Seeds Nearly Normalized renal Histology. Minimal Glomerular Changes are Seen - PAS 400X. (1D-Group IV) Ajwa Fruit Showed Less Significant Effect. Moderate Changes in Glomeruli and Tubules are Visible - PAS 100X.*

In current study, treatment with Ajwa seed and fruit ameliorated relative kidney weight and glomerular size. Our findings are in line with results of Abdelaziz who reported that treatment with Hayani seed aqueous suspension restored the relative weight of kidneys in streptozotocin induced diabetes in rats in 4 weeks time.⁹

Our results of other histopathological indicators showed noticeable presence of capillary congestion, mesangial and glomerular hypertrophy, tubointerstitial fibrosis, glomerular basement membrane thickening along with fairly diffuse glomerulosclerosis in diseased group as compared to control.

Our results are comparable to a study in which oxidative stress produced by alloxan caused severe diabetes. Prolonged hyperglycemia and severe oxidative stress in untreated diabetes lead to micro as well as macro-

angiopathy. Renal vacuolar changes occurred in tubular cells, glomerular mesangium increased and average weight of kidney and size of glomeruli increased in diabetes mainly due to glycogen accumulation, protein synthesis and lipogenesis. Process of glycation lead to degradation of extra cellular matrix and tubointerstitial fibrosis.¹⁴

Treatment with Ajwa seed markedly improved all histological parameters while Ajwa fruit showed minimal to modest improvement in histological characteristics of renal injury. Our results are comparable to a latest study in which researcher found out that date seed powder suspension restored normal architecture of glomeruli and tubules in diabetic nephropathy by streptozotocin.⁹ Previously Ali A demonstrated that Ajwa flesh alleviated Ochratoxin induced tubointerstitial injury.¹⁵

Few other researches found out the preservation of renal tubular epithelial lining along with alleviation of angiopathy and proximal tubular damage in renal injury by carbon tetrachloride and gentamycin respectively.^{16,17}

A massively growing data has demonstrated that p dactylefera is rich in antioxidants and has immense free radical scavenging activities. Date fruits and seeds both are rich in most excellent absorbable polyphenols, carotenoids, minerals and flavonones and all of these have strong antioxidant potential.¹⁸ Polyphenols have proved their efficacy in treating diabetic complications in previous studies P-coumaric acid, gallic acid and cinnamic acids are key phenols and present up to 35.9 mg caffeic acid equivalent per 100gram fresh weight.¹⁹ Dates seeds have shown their ability to enhance antioxidative enzymes in body like catalase, glutathione-transferase and superoxide dismutase.⁹

Ethnobotanical research data found that Ajwadata contain maximum nutrients, antioxidants and polyphenols. Zinc(1.91mg/g), potassium (7.4mg/ 100g), magnesium (59mg/100g), calcium (57.5g/ 100g), iron (23.5/100g) and phosphorus (7.3mg/100g) are the main minerals present in large quantity in Ajwa seed and flesh.²⁰ Ajwa pits have remarkable amounts of polyphenols as compared to fruit.²¹ Ajwa flesh has highest nitric oxide scavenging activity²² while seed extracts of Ajwa is highest in DPPH (3932mgGAE/ 100g) & ABTS (2956mgQEC/100g) activity compared to fruit.²¹ Active flavonoids present in Ajwa seed and fruits are Iso-quercetin, apigenin, quercetin,

luteolin and rutin.²³ Natural polyphenols and rutin have already established their role in prevention of diabetes mellitus through effective antioxidant activities.²⁴

Researchers found the immense improvement by quercetin alone and along with insulin in tubular necrosis and glomerular basement thickening in streptozotocin provoked diabetes in rats. In addition, dates increase insulin secretion, decrease insulin resistance and inhibit alpha glucosidases and amylase activity and thus by retarding the hydrolysis of carbohydrates it helped in treatment of diabetes mellitus.²⁵

In view of above observations, protective effects of both seeds and fruit of Ajwa date may be attributed due to the presence of strong antioxidants and other phytoelements.

Conclusion

Study displays that Ajwa date (*Phoenix dactylifera*) facilitated alleviation of renal deterioration by protecting the tubular, vascular and glomerular structures from oxidative damage. Treatment with Ajwa seed diet significantly reduced relative kidney weight, glomerular diameter and histological features of diabetic kidney. Further studies are required for the detection and isolation of key components which are responsible for nephroprotective effect. Human studies and studies on other diabetic complications may be conducted with varying doses and duration of Ajwa seed and fruit.

Conflict of Interest: None

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Authors Contribution

- II:** Conceptionlization of Project
II,MM: Data Collection
II,NF,AM,AW: Literature Search
II,AM,AW: Statistical Analysis
II,NF: Drafting, Revision
II,MM,AM,AW: Writing of Manuscript

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