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Editorial

Educating Tomorrow's Doctors

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Most worthy medical schools undertake curriculum review and reform from time to time. It often begins with enthusiasm but soon reveals difficult, unresolved questions. Among the most fundamental: What is the single most important attribute tomorrow's doctors must have? Defining this is not just an academic exercise; it shapes the doctors we train and, ultimately, the future of the profession itself.

The answer is not straightforward. The list of contenders is long and has shifted over time. Knowledge, of course, is essential; doctors are no longer barber-surgeons. Critical thinking and the ability to apply the scientific method help doctors guide patients through a landscape crowded with misinformation. Clinical competence, too, is vital, as are the clinical communication skills that are proven to result in better patient outcomes. In the UK, different attributes have risen and receded like tides: lifelong learning, reflective practice, patient care, and, more recently, kindness. In an increasingly interconnected world, diversity, cultural competence, and an international perspective have become essential attributes. Meanwhile, in Western healthcare systems, the increasing marketisation of care has placed the most vulnerable at greater risk, making patient advocacy and public health once again essential skills for doctors.

All these qualities are important, and all should be cultivated - but without a single, defining priority, curriculum design risks becoming a spinning top, expending enormous energy yet making little real progress. An extensive list of desirable attributes may look impressive in a curriculum document, but without a clear guiding principle, it offers no real direction. A singular focus does not diminish the importance of other attributes; rather, it provides a framework for how they should be applied in practice. Choosing the most important attribute for tomorrow's doctors requires looking ahead and also looking back. Today's graduates will still be practicing in 50 years, and the changes their predecessors have faced offer a glimpse of what lies ahead.

In the last fifty years, ultrasound, CT, and MRI have shifted from research tools to routine investigations; laparoscopic surgery and interventional radiology have appeared and then revolutionised treatment; and our understanding of viruses and viral disease has developed exponentially. As late as 1985, an early description of HIV ('slims disease') in The Lancet reassured doctors that 'there is no clear evidence to implicate other possible means of transmission, such as ... re-used injection needles'.[1] Today, this seems unthinkable, yet at the time, it reflected mainstream thought.

Beyond scientific advances, the very role of the doctor has shifted. The internet and mobile data have decentralised medical knowledge, eroding the traditional model of the doctor as the sole authority. The profession has had to redefine itself, not just in response to new discoveries, but in response to changing societal expectations. Future doctors will face even greater shifts - some predictable, others currently unimaginable. Fixed knowledge cannot sustain a lifetime of practice; medical education must prepare graduates to navigate and lead in a landscape of relentless change.

Medical revolutions are inevitable, often unfolding with remarkable speed. When germ theory replaced miasma theory, entire generations of physicians had

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to abandon their fundamental understanding of health and disease. By 1880, the idea of infectious agents remained contested, yet within 30 years, it had reshaped medical science, practice, and education entirely. If current foundational knowledge is overturned just as swiftly in the future, will graduates be ready to adapt, or will they resist, as many did in previous revolutions?

In terms of attributes, then, above all, graduates need to be prepared for profound levels of change during their working lifetimes. Above all, they must be lifelong learners. On this issue, Osler stated that "More clearly than any other, the physician should illustrate the truth of Plato's saying-that education is a life-long process".[2] Whilst widely and consistently accepted in postgraduate training, lifelong learning is often neglected in undergraduate education - precisely where it must begin.[3] Once central to medical education, lifelong learning has steadily slipped down the list of priorities, eclipsed by immediate, competency-based objectives. This shift reflects a broader problem: a growing preoccupation with measuring the measurable, rather than fostering the habits of intellectual curiosity that sustain a doctor's learning for life. Encouraging students to become lifelong learners is not easy. It involves teaching them how to learn (study skills) and teaching them how to actively manage their learning (metacognition). There are extensively researched and validated methods to do this, however these alone are not enough.

Beyond skills and strategies, medical teachers must also inculcate in students the understanding that knowledge is not fixed, but fluid, and that knowledge is not held by the school and passed down to its students, but rather that it is constructed as the learners make sense of what they learn and what they experience. Unfortunately, most students join university with a simple binary view of truth, and the route to intellectual maturity is challenging and only completed by some.[4] If a student graduates believing that they need a teacher to learn, or graduate unable to deal with uncertainty, they will never become lifelong learners.

Paulo Freire critiqued the 'banking model' of education, where "knowledge is a gift bestowed by those who consider themselves knowledgeable upon those whom they consider to know nothing" (p 72).[5] He argued that this approach not only stifles critical thinking but is also a means through which power is maintained, reinforcing the idea that knowledge belongs to those in authority rather than being co-created through dialogue and experience. Traditional medical education has long operated under this model, where expertise is something delivered rather than questioned.

If medical education is to produce lifelong learners, how we teach is just as important as what we teach. Each time a definitive answer is given without acknowledging uncertainty, each time authority is asserted without inviting questioning, and each time debate or dissent is discouraged, the idea is reinforced that knowledge is fixed and learning is passive. We, the educators of tomorrow's doctors, face a challenge not merely to model a different way of thinking, but to believe in it. Preparing doctors for a lifetime of learning requires more than accepting uncertainty; it must be valued. Questioning must not only be permitted but encouraged, and adaptability must not only be taught but embodied in everything we do.

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Original Article

Correlation of Neutrophil-to-Lymphocyte Ratio with Waist Circumference, Insulin Resistance and Lipid Profile in Metabolic Syndrome and Healthy Controls

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Abstract

Background: Metabolic syndrome encompasses a spectrum of interconnected derangements, such as central adiposity, dyslipidemia, insulin resistance and high blood pressure. Low-grade chronic inflammation has a major contribution in the onset and progress of metabolic syndrome. The neutrophil-to-lymphocyte ratio is a well-recognized predictive index for various inflammatory disorders.

Objective: To determine the correlation of neutrophil to lymphocyte ratio with insulin resistance, waist circumference, serum triglycerides and high-density lipoproteins in metabolic syndrome and healthy group.

Methodology: This was a cross-sectional study undertaken at University of Health Sciences Lahore, from October 2019 to September 2022. Approval was obtained from the Ethical Board of the University of Health Sciences. . The subject recruitment was from the Endocrine and Diabetes Clinic of Sheikh Zaid Institute, Lahore. Anthropometric measures and biochemical variables were determined. Data was analyzed by the software; SPSS 27.

Results: The present study comprised of 90 patients diagnosed with metabolic syndrome and 50 controls. In both groups, only male patients were present. The median (IQR) age of the participants with and without metabolic syndrome was found to be 44(40-49.5) and 41(43-49) respectively. The waist circumference, systolic as well as diastolic blood pressure was higher substantially in metabolic syndrome group compared with the healthier ($p<0.001$). Fasting serum glucose, insulin and triglycerides showed a significant difference among both groups statistically ($p<0.001$). There was a positive correlation of neutrophil to lymphocyte ratio with waist circumference ($p=0.006$) and HOMA-IR ($p=0.005$) in metabolic syndrome group and significant inverse relation with high density lipoproteins ($p=0.007$) in healthier ones.

Conclusion: The positive correlation of neutrophil to lymphocyte ratio with insulin resistance and waist circumference in metabolic syndrome highlights the role of chronic inflammation in the disease process.

Keywords: Neutrophil to lymphocyte ratio, Insulin resistance, Chronic inflammation

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Introduction

Metabolic syndrome (MetSy) a complex multifaceted disorder is characterized by a spectrum of interconnected derangements, such as central adiposity, dyslipidemia, insulin resistance and

high blood pressure. It profoundly increases the susceptibility to heart diseases and diabetes type2. As a non-infectious chronic disease, prevalence of MetSy in Pakistan is 33%. Its pooled burden in South Asian region ranges between 17 to 32.5% whereas its global burden is 25 %.[1,2] Low-grade chronic inflammation by disrupting normal metabolic pathways has a major contribution in the onset and progress of MetSy. Prolonged inflammation drives adipose dysfunction that leads to oxidative radical stress, insulin non-responsiveness and disseminated inflammation. Insulin resistance has a prime role in ignition and progression of metabolic dysregulation. Multiple pathological derangements, including imbalance in hepatic lipid and glucose homeostasis, excess free fatty acids (FFAs) release from adipose organs, impaired skeletal glucose uptake, and disrupted pancreatic insulin secretion, contribute to the initiation of central adiposity or insulin resistance. Resistance to insulin action in adipose organs promotes lipolysis resulting in release of free fatty acids. These agents result in lipid accumulation in liver, which selectively hampers insulin action. This results in dyslipidemia picture with elevated triglycerides and low high-density lipoproteins (HDL) in the blood. Disruption of insulin signaling pathways are mainly responsible for non-responsiveness of target areas to insulin action.[3,4]

Many studies underscore the role of inflammation in tissue or area related insulin non-responsiveness. The neutrophil-to-lymphocyte ratio (NLR) is a well-recognized predictive index for various inflammatory disorders.[5] Neutrophil activation contributes to the recruitment of diverse cell types involved in both acute and chronic inflammation, affecting outcome of disease. Neutrophilic to lymphocytic ratio obtained after dividing total neutrophil count by lymphocyte count as given in blood report has emerged as an early marker for diagnosis and prediction of MetSy.[6] Higher NLR level has been observed in insulin resistance endorsing it a state of subclinical inflammation. Previous studies have reported higher NLR values in diabetic patients with a greater likelihood of insulin resistance.[7]

Comprehending inflammation as a root cause of MetSy may navigate the way for precise therapeutic trials aimed at lowering inflammation and elevating metabolic health. As a cost-efficient inflammatory marker, NLR carries potential for the preliminary prediction of MetSy.

The objective of this study was to determine the correlation of NLR with insulin resistance, waist circumference, serum triglycerides and high-density lipoproteins in MetSy and healthy group.

Methodology

This was an analytical and cross-sectional study undertaken at University of Health Sciences Lahore from October 2019 to September 2022.

Ethical consideration: Approval was obtained from the Ethical Board of the University of Health Sciences [UHS/REG-19/ERC/3219] Dated: 29/11/2021. Informed written consent was obtained from the participants, and the confidentiality of their data was clearly explained.

This study included 140 subjects. Calculation of sample size was done with the following equation from WHO calculator.

$$n_1 = \frac{\left(Z_{1-\beta} + Z_{1-\frac{\alpha}{2}}\right)^2 (\sigma_1^2+\sigma_2^2)}{(\mu 1-\mu 2)^2}$$

Z1-β is the power of study 90% and Z 1-α/2 is level of significance 0.05

Minimum sample size was 50 for each group. In the present study, there were 90 cases of metabolic syndrome (Group A) and 50 controls (Group B)

The sampling technique of convenience sampling was adopted. The subject recruitment was from the Endocrine and Diabetes Clinic of Sheikh Zaid Institute, Lahore. The MetSy cases were selected in line with IDF (International Diabetes Federation) criteria . The medical record of the recruiter was evaluated for other concomitant ailment. There are different criteria for the determination of MetSy.

Inclusion Criteria:

As per the rules of IDF, MetSy is present if a subject has central obesity reflected by waist circumference ≥90cm in men, triglycerides ≥1.7 mmol/L or on specific lipid lowering drugs; HDL-cholesterol level ≤1.03 mmol/L in males; elevated blood pressure ≥130/85 or on antihypertensive; fasting plasma glucose ≥5.6 mmol/L or taking anti-diabetics.[8]

Exclusion criteria:

All those cases of MetSy were excluded who had evidence of any of the infectious and inflammatory state such as chronic liver disease, end-stage renal disease, chronic infection or malignancies. Controls were non-blood related attendants of the cases or healthy subjects of hospital.

After getting the written informed consent, every subject was assessed. Blood pressure and waist circumference was recorded by the standard method . Waist circumference (in centimeters) was measured in a horizontal plane midway between the costal margin and iliac crest at the end of normal expiration by a non-stretchable measuring tape.[9] Patients with overnight fast of 8 to 10 hours were counselled for collection of blood sample of 5 ml. Sample was collected in vacutainers of 5 ml and and serum was extracted in the laboratory. It was stored at -400C. Serum insulin levels were measured by Enzyme-Linked Immunosorbent Assay (ELISA) kit (Bio-Rad Laboratories, Hercules, CA, USA). Fasting blood glucose was measured by glucometer. Serum triglycerides and HDL were estimated with the corresponding kits by the colorimetric method (Randox kit). Insulin resistance was calculated by homeostatic model assessment for insulin resistance (HOMA-IR) using following equation.[10]

HOMA-IR=(Fasting plasma glucose (mmol/l)× Fasting plasma insulin (mU/l))/22.5

Statistical Analysis

The data was analyzed by SPSS 27 (IBM Corp. Released 2020. IBM SPSS Statistics for Windows, Version 27.0. Armonk, NY: IBM Corp). To assess the data distribution, Shapiro-Wilk's stats for normality was conducted. Data distribution was skewed as p-value was less than 0.05. Study variables were summarized as median showing central tendency along with interquartile range (IQR) showing dispersion. Non-parametric comparison tests the Wilcoxon Rank Sum was used to compare continuous parameters. Spearman correlation was employed to measure the correlation of continuous quantitative variables. A p of less than 0.05 was of statistical significance.

Results

The present study comprised of 90 patients diagnosed with MetSy and 50 controls. In both groups, only male patients were present. The median (IQR) ages of the group of patients with and without MetSy were found to be 44(40-49.5) and 41(43-49) respectively. The systolic as well as diastolic blood pressure was higher substantially in the cases of MetSy compared with the healthier ones (p<0.001). The median values of waist circumference was higher in cases compared to the controls. Fasting median serum glucose, insulin, triglycerides, had shown a significant difference among both groups. Comparison of study variables in given in Table-I.

Table I: *Comparison of study variables between metabolic syndrome and healthy group*

Study variables	Metabolic syndrome	Healthy group	p-value
	n= 90	n=50	
Age	44 (40-49.75)	41 (34-49)	0.08
Waist circumference in cm	99 (93-106)	84 (75-88)	<0.001*
Serum glucose in mg/dl	142 (120-176)	90 (80-99)	<0.001*
Serum insulin in µI U/ml	22 (12.95-33.6)	8.8 (6-13.5)	<0.001*
HOMA-IR	6.35 (3.97-10)	1.79 (1.27-3.04)	<0.001*
Total leucocyte count X 10^3 /µL	8.85 (7.27-10.30)	7.34 (6.15-8.23)	<0.001*
Total neutrophil count X 10^3 /µL	5.5 (4.1-6.92)	4.4 (3.5-4.9)	0.001*
Total lymphocyte count X 10^3/µL	2.5 (2.0-3.9)	2.2 (1.9-2.9)	0.062
Neutrophil to lymphocyte ratio	2.29 (1.82-3)	1.76 (1.52-2.32)	0.005*
Serum triglycerides in mg/dl	213 (161-203)	150 (135-190)	0.001*
Serum HDL in mg/dl	37.5 (31-43.2)	39 (35-46)	0.062

The p-value is determined by Wilcoxon Rank sum test. A value less than 0.05 is of significance statistically. (n= number of participants)

There were positive correlational results of NLR with waist circumference and HOMA-IR in MetSy group and a significant inverse relation with HDL in healthier ones. (Table II and Figures I & II)

Table II: *Correlation of neutrophil to lymphocyte ratio with study variables*

	HOMA-IR	Waist circumference	Serum triglycerides	Serum HDL
Correlation of neutrophil to lymphocyte ratio with study variables in metabolic syndrome group				
Rho value	0.289	0.285	0.145	0.168
p-value	0.005*	0.006*	0.477	0.335
Correlation of neutrophil to lymphocyte ratio with study variables in healthy group				
Rho value	0.245	0.14	0.022	-0.378
p-value	0.08	0.332	0.14	0.007*

The p-value is determined by Spearman test. A value less than 0.05 is of significance statistically.

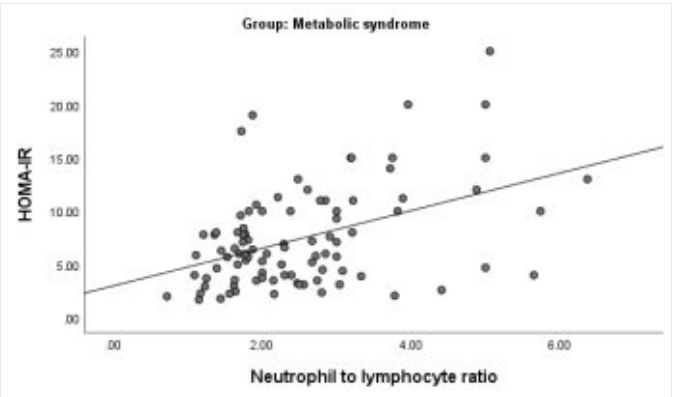

Figure-I: *Correlation of neutrophil to lymphocyte ratio with HOMA-IR in metabolic syndrome.*

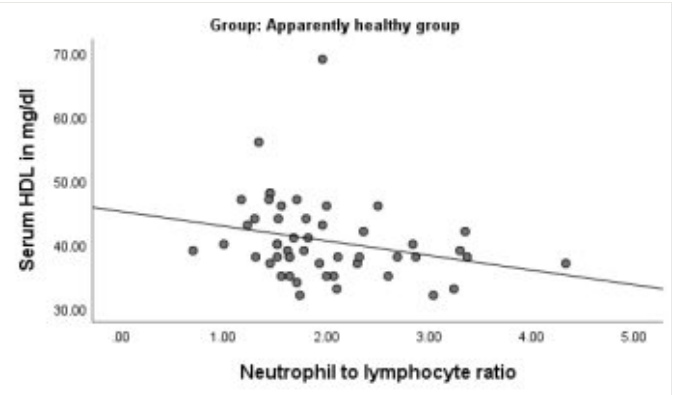

Figure-II: *Correlation of neutrophil to lymphocyte ratio with serum HDL in healthy group*

Discussion

The present study revealed considerably higher NLR, insulin resistance, and waist-circumference in cases as compared to the controls. Furthermore, NLR was positively related with insulin resistance and waist circumference in the diseased group. These results are in agreement with the previous studies conducted in Pakistan and neighboring areas.[6,7,11] The current study is conducted on male patients only, however a study conducted in patients with gestational diabetes also revealed considerable association of NLR with insulin resistance and body mass index.[12] Another previous study observed relationship between new measures of inflammation such as NLR, platelet count, neutrophil count and insulin resistance in obese children. Increased leucocyte count and elevated NLR in obese or overweight boys serve as biomarker of insulin resistance and were endorsed to be undertaken when evaluating the risk of potential complications, such as type 2 diabetes mellitus.[13] A systematic review revealed the relation of NLR with poorly controlled glycated hemoglobin in type2 diabetics. NLR was considerably higher in the group exhibiting poor control of glycosylated hemoglobin as compared to the one with good control.[14] Another study revealed that NLR correlated positively with HbA1C in type2 diabetics.[15] These studies reflect that insulin resistance and hyperglycemia lead to oxidative stress thus contributing towards chronic inflammation; which in turn results in neutrophilia and relative fall in lymphocytic count. There are various postulated mechanisms, by which insulin resistance leads to immune dysregulation. The mechanisms include release of pro-inflammatory cytokines such as interleukin-6 and tumor necrosis factor, which promote production of neutrophils.[16,17] Increased waist circumference is a prime indicator of central obesity and is correlated strongly with insulin resistance and chronic low-grade inflammation. Visceral fat being a dynamic endocrine organ, release pro-inflammatory cytokines (e.g., TNF-α, IL-6, visfatin), which increases neutrophil production and reduce lymphocyte count, leading to an elevated NLR.[18,19] Central obesity is also linked to poor glycemic control, contributing to higher HbA1c levels. An increasing level of NLR indicate worsening of glucose regulation and risk of cardiovascular complications.[20-22] This relation underscores the significance of controlling blood glycemic levels to reduce inflammation and mitigate

the likelihood of diabetes-related complications. It also implies that monitoring NLR in diabetic patients may provide further insight into their inflammatory status and overall progress.[23,24]

Conclusion

The positive correlation of neutrophil to lymphocyte ratio with insulin resistance and waist circumference in metabolic syndrome highlights the role of chronic inflammation in the disease progression.

Limitations and Recommendations: The study has limitations as patients were on medications for control of blood pressure and glucose levels which may affect the results. Moreover cross-sectional study does not provide causal relationship. Further longitudinal studies are needed to establish causality and explore potential therapeutic implications.

Conflict of Interest: *None*

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Authors Contribution: All the authors contributed equally, in accordance with ICMJE guidelines and are accountable for the integrity of the study.

FA: Conception, design, data analysis, initial and final draft making, accountable.

HART: Analysis and interpretation, initial and final draft making, proof reading

NZ: Data acquisition, analysis, drafting and final revision, accountable

HSK: Revising the initial and final draft, data collection and data anallysis, accountable.

Original Article

Evaluation of Periodontal Health in Diabetic Patients: Influence of Glycemic Control and Diabetes Duration Using the Community Periodontal Index – A Longitudinal Study

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Abstract

Background: Diabetes is a long-term metabolic disease with consequences for periodontal health. However, various studies have established a link between diabetes and periodontal health. In this regard very limited research has been done to investigate the impact of duration of diabetes and glycemic index on periodontal health.

Objective: To evaluate glycemic control (HbA1c levels) and diabetes duration on periodontal health using the Community Periodontal Index (CPI).

Methodology: The duration of the study was one year and six months after the approval of synopsis from ethical review board.-Based on their glycemic control, 225 diabetic patients were split into three groups: effectively controlled (HbA1c <7%), mildly controlled (HbA1c between 7 and 9%), and inadequately controlled (HbA1c >9%). Periodontal health assessment was performed using the CPI at three time points: baseline, six months, and twelve months.

Results: The study sample was 225 participants. The severity of periodontal disease was higher in diabetic patients with poor glycemic control. Over 12 months, CPI of the poorly controlled group increased to 85%, while the mildly controlled group increased to 55%, and the well-controlled group increased to 30%. A significant correlation was found between HbA1c levels and CPI scores ($r=0.72$, $p<0.001$), and between diabetes duration and CPI scores ($r=0.68$, $p<0.001$).

Conclusion: The present study suggests a significant effect of glycemic control (HbA1c levels) and diabetes duration on periodontal health assessed by using the Community Periodontal Index (CPI).

Keywords: Diabetes mellitus, periodontal disease, Glycated hemoglobin A, Community Periodontal Index (CPI), longitudinal study.

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Introduction

Diabetes mellitus (DM) is a worldwide health concern, currently over 537 million adults are being affected with this problem, and its incidence is expected to rise in the coming decades. A

73% prevalence of periodontitis was reported in diabetic study population, with a statistically significant association found with age.[1] It is a systemic metabolic disorder characterized by high blood sugar levels that may result from inadequate insulin synthesis or insulin resistance. Uncontrolled diabetes leads to a myriad of complications, including neuropathy, nephropathy, retinopathy, cardiovascular diseases, and periodontal disease.[2,3] Beyond its systemic effects, diabetes mellitus has significant implications for oral health. Individuals with diabetes commonly experience xerostomia (dry mouth), altered taste perception, an increased risk of dental caries, gingival inflammation, and delayed wound healing.[4,5] Periodontal disease, is a common chronic inflammatory condition. It is one of the most serious oral health issues among diabetic patients. It affects the gingiva, periodontal ligament, and alveolar bone.[6] At the time of onset, it appears as gingivitis, but if treatment is not received, it can develop into periodontitis and result in tooth loss. Research has indicated that diabetes and periodontitis share a bidirectional relationship, where poorly controlled diabetes exacerbates periodontal disease.[7-9]

The evaluation of periodontal health in both diabetic and non-diabetic populations, standardized tools such as the Community Periodontal Index (CPI) are widely utilized. Developed by the World Health Organization (WHO) in collaboration with the FDI World Dental Federation, the CPI serves as an effective and globally recognized method for assessing periodontal status in epidemiological studies[10]. Its simplicity, cost-effectiveness, and reproducibility make it a valuable tool for large-scale evaluations of periodontal disease prevalence.[11,12] Various studies have demonstrated that people with diabetes have a high risk of periodontal disease as compared to non-diabetic individuals, and poor glycemic control has been particularly linked to a greater likelihood of periodontal complications, including deeper periodontal pockets, higher attachment loss, and more extensive alveolar bone resorption.[13,14] Despite the well-established association between diabetes and periodontitis, there are limited studies reporting the incidence and severity of periodontal disease in relation to glycemic control in diabetic patients within local populations.[15] Although several cross-sectional studies have demonstrated a link between diabetes and periodontal disease, few investigations have examined how periodontal disease develop over time in patients with diabetes.[16] The impact of glycemic control and diabetes duration on periodontal disease severity has not been investigated adequately. This research attempts to close this gap by conducting a longitudinal evaluation of periodontal health in diabetic patients, using the Community Periodontal Index (CPI) over a period of twelve months.

Methodology

The study was carried out in Madina Teaching Hospital Faisalabad in the periodontology department from 1st Nov 2022 to 30th April 2024 (total duration 1year and six months after ethical approval). Patients were observed and followed over a 12-month period. The data was collected using non-probability convenient sampling technique. The Community Periodontal Index (CPI) was used to evaluate the course of periodontal disease in patients with diabetes.

Ethical Consideration:

Ethical approval was obtained under IBR reference: TUF/IBR/148/2022, Dated: 25/10/2022. Informed written consent was obtained from the participants and confidentiality was maintained. Cochran's formula for prevalence studies was used to calculate the study's size of the sample. The initial calculated sample size was 369, assuming a 60% prevalence of periodontal disease in diabetic patients, a 95% confidence level (Z = 1.96), and a 5% margin of variation (d = 0.05)[17]. However, considering feasibility, study duration, and patient availability at the study site, the final size of sample was adjusted to 225 participants with a statistical power of 80% to detect significant differences in periodontal disease progression across glycemic control.

Participants were enrolled based on inclusion and exclusion criteria.

Inclusion criteria: The inclusion criteria required participants to have a confirmed diagnosis of Type II diabetes mellitus for at least one year, between 30 to 75 years of age, have a minimum of 20 remaining teeth, divided into six sextants and the CPI recording was performed on the index teeth that is No. 17-16, 11, 26-27, 36-37, 31, 46-47. It was made sure that participants have not undergone any periodontal treatment in the past six months.

Exclusion Criteria: Individuals who were pregnant or lactating, undergoing radiotherapy or immunosuppressive therapy, diagnosed with

autoimmune diseases, or had taken antibiotics in the past three months were eliminated from the study. A maximum of 225 participants were recruited and categorized according to their glycemic control and diabetes duration. Glycemic control was determined using HbA1c levels, with participants classified into three groups: well- controlled diabetes (HbA1c <7%), mildly controlled diabetes (HbA1c 7–9%), and inadequately controlled diabetes (HbA1c >9%). Additionally, patients were stratified into 3 groups on the basis of duration of diabetes less than five years, between five to ten years, and greater than ten years.[18] Patients were observed and followed up over a 12-month period. Periodontal health assessment was performed using the CPI at three time points: baseline, six months, and twelve months. The oral cavity was divided into six sextants, and index teeth (17, 16, 11, 26, 27, 36, 37, 31, 46, 47) were inspected to determine the periodontal status. The CPI scoring system included five categories: Code 0 (healthy gingiva), Code 1 (gingival bleeding), Code 2 (appearance of calculus), Code 3 (shallow periodontal pockets of 4–5 mm), and Code 4 (deep periodontal pockets of ≥6 mm).[19]

Statistical Analysis

SPSS version 24 was used for data analysis. The Chi-Square test was applied to assess the gender distribution across the three groups and to analyze the prevalence of CPI Codes 3 and 4 at baseline, six months, and twelve months. While repeated-measures ANOVA was utilized to examine the evolution of periodontal disease over time. Additionally, the relationship between HbA1c levels, the length of diabetes, and periodontal disease was investigated using Pearson correlation analysis.

Results

The study cohort consisted of 225 participants, categorized into four age groups: under 40, 40-49, 50-59, and 60 years and above. The overall gender distribution shows a slight male predominance, with 56.4% males and 43.6% females. The male-to-female ratio is consistent across the age groups, ranging from 1.17:1 to 1.38:1 in various age groups. Despite the variations, the overall male-to-female ratio remains approximately 1.3:1, with 127 males and 98 females. The age distribution highlights a relatively balanced representation across all age categories while introducing subtle differences across age groups. (Table I)

Table I: *Demographic Data (Age and Gender Distribution) (n=225)*

Age Group (Years)	Total (n)	Male (%)	Female (%)	Male (n)	Female (n)	Male-to-Female Ratio
<40	50	57	43	29	21	1.38:1
40-49	70	58	42	41	29	1.41:1
50-59	55	54	46	30	25	1.20:1
60+	50	53.5	46.5	27	23	1.17:1
Total	225	56.4	43.6	127	98	1.30:1

n=Number of Participants, %=percentage

The study cohort of 225 participants was divided into three groups based on glycemic control. The mean age of participants was 50.2 ± 7.5 years in the well-controlled group (HbA1c <7%), 52.8 ± 8.2 years in the mildly controlled group (HbA1c 7–9%), and 54.1 ± 9.3 years in the inadequately controlled group (HbA1c >9%) and it was not statistically different

Table II: *Diabetes Duration and Age Across Glycemic Control Groups (n=225)*

Group	Mean Age (yrs) & SD	Diabetes Duration (0–5 yrs) & SD	Diabetes Duration (5–10 yrs) &SD	Diabetes Duration (>10 yrs) & SD
Well-Controlled (HbA1c <7%)	50.2 ± 7.5	Mean: 2.3 ± 1.2	Mean: 7.1 ± 1.5	Mean: 12.0 ± 2.5
Mildly Controlled (HbA1c 7–9%)	51.8 ± 8.2	Mean: 2.7 ± 1.4	Mean: 7.3 ± 1.8	Mean: 12.3 ± 2.8
Inadequately Controlled (HbA1c >9%)	53.1 ± 9.3	Mean: 2.5 ± 1.6	Mean: 7.6 ± 2.1	Mean: 13.0 ± 3.2
p value	0.08			

n=Number of Participants, SD=standard deviation, yrs= years, p value calculated by ANOVA, p value < 0.05 considered significant

across the three groups (p value = 0.8). The diabetes duration for each glycemic control group spans three categories: 0–5 years, 5–10 years, and more than 10

Table III: *Association between Gender Distribution and Prevalence of CPI Code 3 or 4 with HbA1c Groups*

Group	Male (%) (n)	Female (%) (n)	Total (n)	Prevalence at Baseline (%)	Prevalence at 6 Months (%)	Prevalence at 12 Months (%)	p-value (Gender Distribution)	p-value (Baseline)	p-value (6 Months)	p-value (12 Months)
Well-Controlled (HbA1c < 7%)	60(45)	40(37)	82	20	25	30	0.93	0.2	0.047	0.015
Mildly Controlled (HbA1c 7–9%)	61.3(46)	38.7(35)	81	40	50	60	-	0.2	0.047	0.015
Inadequately Controlled (HbA1c > 9%)	65.3(36)	34.7(26)	62	60	75	85	-	0.2	0.047	0.015

n=Number of Participants, CPI= Community Periodontal Index, p value calculated by Chi square test, p value < 0.05 is considered significant

years, with varying means and standard deviations reflecting the diversity in how long participants have had diabetes (Table II).

The Chi-Square test was applied to assess the gender distribution across the three glycemic control groups: The male-to-female ratios were relatively consistent across the groups, with 60% males in the well-controlled group, 61.3% in the mildly controlled group, and 65.3% in the inadequately controlled group, while females made up 40%, 38.7%, and 34.7% in each group, respectively. The Chi-Square test for gender distribution yielded a p-value of 0.93, indicating no significant difference in gender across the groups. (Table III). Additionally, the Chi-Square test was used to analyze the prevalence of CPI Codes 3 and 4 at baseline, six months, and twelve months. The prevalence of CPI Codes 3 or 4 was 20%, 40%, and 60% at baseline, 25%, 50%, and 75% at six months, and 30%, 60%, and 85% at twelve months for the well-controlled, mildly controlled, and inadequately controlled groups, respectively. The Chi-Square test results showed no significant difference at baseline, but significant differences in CPI Code 3 or 4 prevalence at both six and twelve months (Figure I).

There was a significant increase in periodontal disease severity over time, with an elevated rate of progression in patients with poorly controlled diabetes. At baseline, 20% of the well-controlled group had CPI Code 3 or 4, which increased to 25% at six months and 30% at twelve months. In the mildly controlled group, the prevalence of CPI Code 3 or 4 was 40% at baseline, rising to 50% at six months and 60% at twelve months. The poorly controlled group exhibited the most severe periodontal deterioration, with 60% of patients showing CPI Code 3 or 4 at baseline, escalating to 75% at six months and 85% at twelve months (Figure-I).

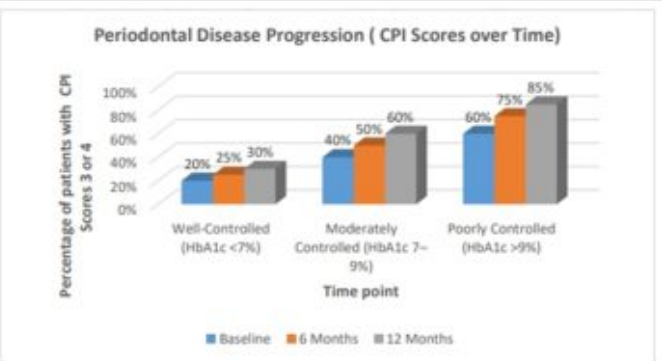

Figure I: *Periodontal Disease Progression Over 12 Months.*

The degree of periodontal disease was found to be

Table IV: *Correlation Analysis Between Variables*

Variable	Correlation Coefficient (r)**	p-value***
HbA1c and CPI Score	0.72	<0.001
Diabetes Duration and CPI*	0.68	<0.001

**CPI: Clinical Periodontal Index.*
***calculated by Pearson correlation,*
****Significant p-values, p value < 0.05 considered significant.*

strongly positively correlated with HbA1c levels. With a p-value of less than 0.001, Pearson correlation ratio (r) between HbA1c levels and CPI score was 0.72, suggesting a statistically significant association. With a p-value of less than 0.001 and an R-value of 0.68, the correlation between diabetes duration and CPI was likewise significant, indicating that a prolonged time span of diabetes is linked to an increased severity of periodontal disease (Table IV).

Discussion

The present study underscores the significant impact of glycemic control and diabetes duration on periodontal health, as measured by the Community Periodontal Index (CPI) over a 12 month period. Our findings reveal that poorly controlled diabetes (HbA1c >9%) and longer disease duration (>10 years) are strongly correlated with the progression of periodontal disease. In contrast to 40% in the mildly controlled group and 20% in the well-controlled group, 60% of diabetics with poorly controlled diabetes had CPI codes 3 or 4 at baseline. The severity of periodontal disease progression with poor glycemic control was highlighted by these numbers, which rose over time and reached 85% in the poorly controlled group at 18 months. In 2021, Stoicescu et al. studied 182 type 2 diabetes patients with generalized chronic periodontitis, assessing glycemic control through HbA1c levels and various periodontal parameters. The study found that patients with poor glycemic control (HbA1c ≥7%) had significantly worse periodontal health, including higher plaque accumulation, probing depth, and clinical attachment loss.[19] In comparison, our study of 225 participants found a significant correlation between HbA1c levels, diabetes duration, and periodontal disease severity. Over 12 months, the poorly controlled group increased to 85%, while the mildly controlled group increased to 55%, and the well-controlled group increased to 30%. Moreover, a significant correlation was found between HbA1c levels and CPI scores, and between diabetes duration and CPI scores. Wu et al., in a meta-analysis, reviewed 53 observational studies and found a higher prevalence of periodontitis among Type II Diabetes patients(T2DM), as reflected in a 0.61 mm deeper periodontal pocket, a 0.89 mm higher attachment loss and approximately 2 more lost teeth, than those without T2DM. They found that T2DM could elevate the risk of developing periodontitis by 34%. The glycemic control of T2DM patients might result in different periodontitis outcomes.[20] This study parallels our finding that diabetic patients with poor glycemic control exhibit worse periodontal outcomes.

In 2023, Nabila et al. reported that individuals who had good glycemic control had better periodontal health compared to those with poor oral hygiene practices.[21] This is in accordance with the results of current study. Santonocito et al. investigated how patients with type 2 diabetes's metabolic status and glycemic control were affected by periodontitis. Researchers found that patients with severe periodontitis had a worse lipid profile and significantly higher HbA1c levels than those with mild or no periodontitis.[22] This aligns with our findings that poor periodontal health is associated with suboptimal glycemic control. Furthermore, studies highlighted the bidirectional association between periodontal disease and diabetes. The researchers found that poor glycemic control in diabetic patients exacerbates periodontal inflammation, leading to increased severity of periodontitis. Conversely, the presence of periodontal disease negatively affects glycemic control, creating a cyclical relationship that complicates disease management. Chen et al. included 23 RCTs in their systematic review and meta-analysis. They reported that after 3 and 6 months, periodontal therapy significantly reduced glycosylated hemoglobin (HbA1c) level (3-month: weighted mean difference [WMD] - 0.514, 95% confidence interval [CI] - 0.730, - 0.298, p = 0.000; 6-month: WMD - 0.548, 95% CI - 0.859, - 0.238, p = 0.000).[23,24] This underscores the necessity for integrated care approaches that address both conditions simultaneously.

The longitudinal design of the current study provides a comprehensive view of periodontal disease progression in diabetic patients over time. By stratifying participants based on HbA1c levels and diabetes duration, the role of poor glycemic control was identified as a risk factor contributing to periodontal deterioration. The correlation analysis further reinforced the results, with HbA1c levels

showing a strong positive correlation with CPI scores, and diabetes duration similarly correlating with periodontal severity. These results are in line with previous research and emphasize the value of including periodontal examinations in regular diabetes care from a clinical standpoint.[25]

Conclusion

This study highlights the significant link between poor glycemic control, longer duration of diabetes, and worsening periodontal health. The findings underscore the importance of recognizing periodontal disease as a common and serious complication of diabetes. Integrating dental professionals into multidisciplinary diabetes care teams is essential to ensure comprehensive management and improved health outcomes. Collaborative care models should prioritize routine periodontal evaluation and intervention as part of standard diabetes management protocols.

Limitations and Recommendations: This was an observational study; therefore, it limits causal inferences. Self-reported data on diabetes management and oral hygiene may introduce bias, and the study did not account for all potential confounders, such as genetic factors or comorbidities. Larger, longitudinal studies are needed to fully comprehend how diabetics' periodontal health and glycemic control are related.

Conflict of Interest: None

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AS: Conception of Idea, Literature Review, Data Acquisition and Analysis, and Final Draft.

SAK: Literature Review, Data Analysis, Final Review.

MM: Literature Search, Data Collection, Draft and Review.

NK: Literature Search, Data Analysis, Drafting the Manuscript and Revision

SI: Literature Search, Data Collection, Draft and Review.

NUH: Literature Search, Data Analysis, Drafting Manuscript and Revision

Original Article

Outcomes of Karydakis Flap Procedure for Primary Pilonidal Sinus Disease at a Teaching Hospital in Pakistan: A Prospective Study of a Single-Arm Surgical Intervention

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Abstract

Background: Pilonidal sinus disease (PSD) of natal cleft is a long-term illness characterized by a blind epithelial tract containing hair, commonly affecting young males with excessive body hair. Various surgical techniques have been developed to treat PSD, yet no universally accepted standard exists.

Objective: To evaluate the clinical outcomes of the Karydakis flap procedure in patients who were diagnosed with primary natal cleft pilonidal sinus disease.

Methodology: This research was carried out at a teaching hospital in Lahore, Pakistan in which 100 patients suffering from primary sacrococcygeal pilonidal sinus disease underwent Karydakis flap procedure. Patient data, including procedure duration, hospital stay, postoperative pain levels, wound infection rates, seroma formation, flap necrosis, and recurrence, were systematically recorded and analysed using SPSS version 21.0.

Results: The results demonstrated favourable outcomes, with an 86% primary healing rate. The average procedure time was 47.50 ± 5.14 minutes, and the average length for hospitalization was 1.87 ± 0.80 days. Postoperative pain was measured by using the Visual Analog Scale (VAS), which had a mean score of 3.45. Surgical site infections were observed in 8% of cases, while 6% experienced seroma formation. No case of flap necrosis was reported, and disease recurrence occurred in only 2% of patients within six months.

Conclusion: Karydakis flap procedure is a reliable and effective surgical approach for treating primary pilonidal sinus disease of the natal cleft. Its design supports faster recovery, minimal postoperative issues, and reduced recurrence, making it a preferred option in clinical practice.

Keywords: Pilonidal Sinus , Karydakis , Surgical Flaps, Complications, Recurrence

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Introduction

Pilonidal sinus disease of the natal cleft is a closed epithelial passage that typically harbours hair and is often present a few inches above the external anal opening, in the natal cleft skin.[1,2] Its highest prevalence is usually found among the young males who have excessive body hair, though it can affect individuals across a wider age range.[1] The condition may present as

an abscess or a draining sinus, often discharging pus or blood.[1,2] Pilonidal sinus disease is more commonly found in men as compared to the women.[3] Karydakis identified three primary factors contributing to its development: an excessive amount of loose hair at the nape of neck and the back, extreme pressure that forces these hair into the skin, and increased susceptibility to infection due to a deep natal cleft.[4] The depth of the natal cleft makes an ideal environment for hair penetration, leading to bacterial contamination.[4] Other significant risk factors include chronic itching, a sedentary lifestyle, genetic predisposition, inadequate hygiene, and excessive body hair. Loose hair can become embedded within the skin of the natal cleft, rolling up to form a nest-like structure that eventually triggers pain and infection.[1,2,5]

The treatment approach for primary natal cleft pilonidal sinus disease varies widely, it could range from wide excision with secondary intention healing to excision followed by some form of flap reconstruction. However, a universally accepted standard surgical method is yet to be established. Most surgical procedures are associated with common complications, including wound infections, seroma formation, and a high recurrence rate. Flap reconstruction techniques aim to address the root cause of pilonidal sinus disease by flattening the intergluteal region.[6,7]

The Karydakis procedure is a reconstructive technique that relies on the superior gluteal and sacral perforators for reinnervation.[5] Research indicates that this flap rotation technique yields better outcomes compared to alternatives like the Limberg and Bascom procedures. It has been linked to a shorter hospital stay, faster recovery, reduced pain levels, higher patient satisfaction, and a significantly lower incidence of wound infections, seroma formation, and recurrence.[8]

The varying perspectives in the medical literature have led to an ongoing debate about the effectiveness of various flap reconstruction methods to treat the sacrococcygeal pilonidal sinus disease. This research aimed to evaluate the results of the Karydakis flap procedure at a teaching hospital in Pakistan. The results of this study will provide important insights to help surgeons to select the optimal surgical technique for treating patients suffering from primary sacrococcygeal pilonidal sinus disease. This study specifically examined variables including the duration of hospitalization, postoperative pain intensity, initial healing success, incidence of surgical wound infections, flap necrosis, development of seroma, and rate of the relapse.

Methodology

This was a prospective study of a single-arm surgical intervention spanning a duration of three years (from January 2022 till December 2024) at Ghurki Trust Teaching Hospital, Lahore, Pakistan.

Ethical Approval: The study was approved by the Ethical Review Board of Lahore Medical and Dental College, Lahore Pakistan via reference number LMDC/13110-12 Dated: 20/12/2021. Informed written consent was obtained and confidentiality was maintained. The first patient was admitted on January 10, 2022, while the last patient was admitted on December 20, 2023. On December 20, 2024, the last follow-up visit for the last participant was conducted. A total of 100 consecutive patients visiting the outpatient department were included in this research through non-probability convenient sampling. Sample size was calculated to detect clinically significant difference of 5 % with 95% confidence and 80% power (https://doi.org/10.1002-/wjs.12492).[9] Each eligible patient was thoroughly counselled about the research, and only those who provided informed consent proceeded with the Karydakis procedure.

Inclusion criteria:

Individuals with the age ranging from 18 years to 60 years and were suffering from primary sacrococcygeal pilonidal sinus disease, no indications for infection or abscess formation were included in this research.

Exclusion criteria:

Individuals with recurrent pilonidal sinus disease, uncontrolled diabetes, non-managed hypertension, renal failure, or immunosuppressive conditions were not the part of this research. Patients deemed unfit for general anesthesia due to pre-existing health

conditions, as indicated by the anaesthesia team, were also not the part of this research.

Statistical Analysis:

Patient data was systematically documented using a structured proforma. A single surgical resident gathered comprehensive medical histories from all participants, while a single consultant surgeon conducted their clinical examinations. Necessary laboratory tests, as required by the anesthesia team for administering general anesthesia, were completed for each patient. All patients gave their informed consent before the surgery.

A single consultant surgeon performed all the surgeries. The surgeon who performed the surgeries was specifically trained in performing this technique. To ensure consistency and minimize bias, the same surgeon was responsible for both pre-operative assessments and post-operative evaluations. Before surgery, hair in the sacrococcygeal area were trimmed on the operating table. All patients received intravenous antibiotics, including 1.2 grams of Amoxicillin with Clavulanic acid and 400 mg of Metronidazole, at the time of induction of anesthesia. The procedures were conducted under general anesthesia, with patients positioned in the prone, jack-knife position. The flap was delineated using a sterile skin marker, after which an elliptical excision was made symmetrically which was positioned at 2 cm to the side of the midline of natal cleft (Figure. I). The excision was made on the side on which most of the tissues were effected or on the secondary sinus openings of the natal cleft skin (Figure. I). All diseased tissue associated with pilonidal sinus disease, along with a portion of healthy normal tissue, was excised to move the final wound closing to the lateral side (away from the midline). A skin flap measuring 2-cm width and 1-cm in thickness was moved from the opposite side of the body to cover the surgically removed area and reconstruct the natal cleft, ensuring the midline was covered with normal healthy skin (Figure. II). To facilitate drainage, the placement of suction drain was carried out in the subcutaneously for all the cases. Intravenous antibiotics were administered for 48 hours postoperatively, followed by a five-day course of oral antibiotics.

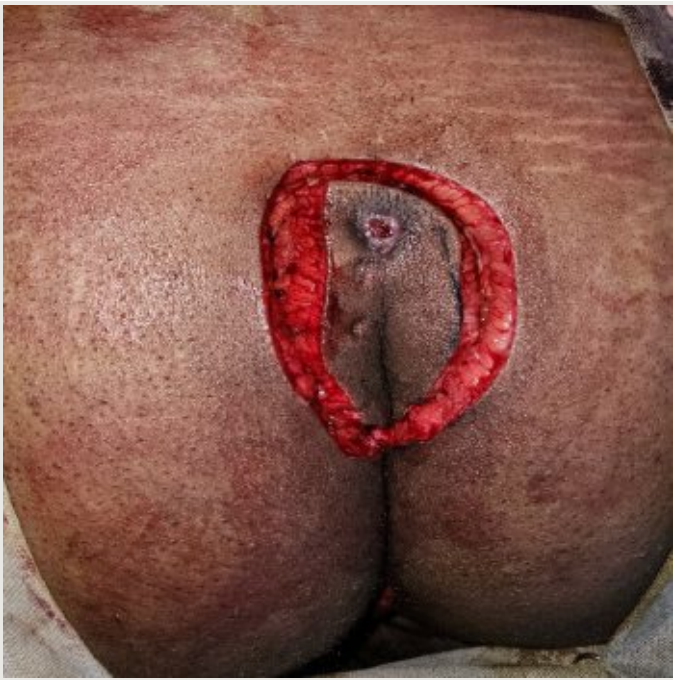

Figure-I: *(Pre-operative)*

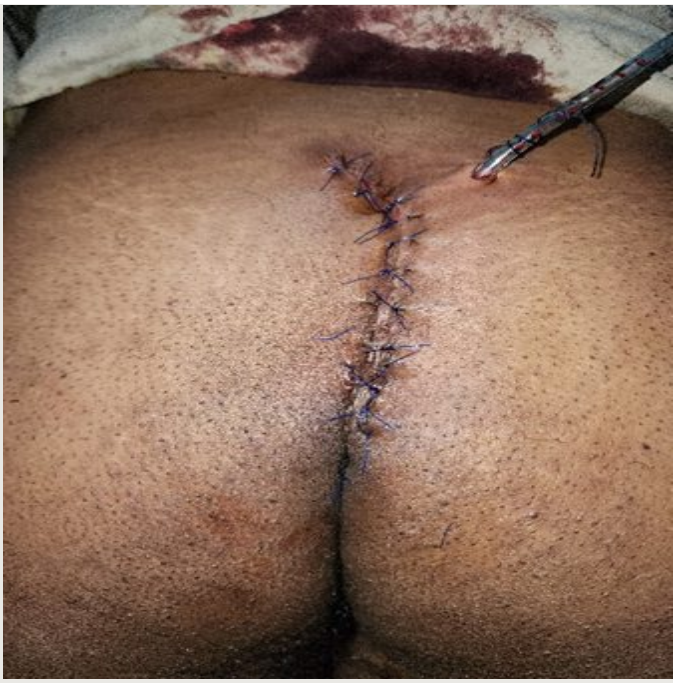

Figure-II: *(Post-operative)*

The duration of surgery was measured in minutes for each patient and the duration for hospitalization was documented hourly. The data of all patients was systematically recorded using a proforma, including all necessary details such as duration of the surgery (in minutes), time for hospitalization (in days), postoperative pain assessment using the Visual Analog Scale (VAS) at 24 hours, as well as

occurrences of flap necrosis, surgical site infections, and seroma development. Patients attended follow-up appointments in the outpatient department on the 7th and 14th postoperative days. Wound infections were evaluated by evaluating clinical signs including redness, erythema, and purulent discharge from the surgical site. Six months after surgery, a third follow-up evaluation was conducted to detect recurrence, which was identified by the recurrently occurring sinus in the natal cleft and by the signs of purulent or discharge of blood during examination. The final follow-up took place at the one-year mark, evaluating recurrence based on the same criteria used at the six-month review. Patients who failed to attend their scheduled follow-ups were contacted and reminded to visit the clinic to document any complications or recurrences.

The version 21.0 of SPSS software was used to carry out the statistical analysis. Numerical variables such as patient age, disease duration, surgical time, and hospital stay length were expressed as mean ± standard deviation (SD). Meanwhile, demographic variables, which included gender, seroma development and the incidences of wound infection were represented as frequencies and percentages.

Table I: *Demographic information of the study participants*

Number of patients	n = 100
Males Frequency (%)	67 (67)
Females Frequency (%)	33(33)
Age of the participants (years) Mean ± SD	26.6 ± 8.6
Duration of the disease (months) Mean ± SD	3.7 ± 1.7

n= Number of Participants, Mean ± SD: Mean ± Standard Deviation

Results

100 patients in total were treated with the Karydakis flap procedure in this research. The demographic information is given in Table I. Patient's ages were ranging from 18 years to 60 years. The duration of the disease was ranging from 1 month to 6 months, with a mean duration of 3.7 ± 1.7 months. The outcome variables of this research are shown in Table. II. The average time of operation was 47.50 ± 5.14 minutes, and the average time of hospitalization was 1.87 ± 0.80 days. Postoperative pain was assessed by administering the VAS after 24 hours of surgery, and the mean score was recorded to be 3.45.

Table II: *Outcomes of the study*

Number of patients	n = 100
Operating time (minutes)	47.50 ± 5.14
Hospital stay (days)	1.87 ± 0.80
Postoperative pain (VAS at 24h)	3.45
Complete primary healing	86 (86%)
Surgical site infection	8 (8%)
Seroma formation	6 (6%)
Flap necrosis	0 (0%)
Recurrence within one year	2 (2%)

n= Number of Participants, VAS = Visual analogue scale

Among all cases, 86% (86 patients) achieved complete primary healing without any complications. Surgical site infections were observed in 8% (8 patients), while 6% (6 patients) experienced seroma formation. There were no instances of flap necrosis. Additionally, 2% (2 patients) with initially successful healing presented with disease recurrence within six months. Every patient was followed up for a total duration of one year after the procedure.

Discussion

Pilonidal sinus disease of the natal cleft is known for its high recurrence rate, leading to prolonged healing and increased treatment costs for patients.[10] Surgeons continue to debate about the most effective treatment approach, as no single surgical procedure has been universally accepted as the gold standard. Various techniques are used, yet all carry a significant risk of complications and recurrence. An ideal surgical procedure should minimize complications, be cost-effective, reduce hospital stays, and lower recurrence rates.[11] Research suggests that reducing recurrence risk requires flattening the natal cleft and ensuring that wound closure is positioned away from the midline. Midline surgical closures are more prone to wound dehiscence, infection, and recurrence.[12,13]

The Karydakis technique offers a reconstructive solution that flattens the natal cleft and ensures lateralised wound closure, promoting faster healing. This procedure involves a large transposition flap with a well-vascularized pedicle, making it a versatile and effective option.[14] Its advantages include ease of design and execution, with the flap size adaptable to the number and location of sinus pits, allowing for tension-free closure and a cosmetically acceptable scar.[15] This method is particularly beneficial for patients with complex pilonidal sinuses featuring multiple pits or those with a history of unsuccessful surgical treatments. To prevent seroma formation and subsequent wound infection, post-operative drain placement is crucial.[5] Additionally, a gradual return to daily activities, routine hair removal from the affected area, and proper wound hygiene play key roles in minimising recurrence.

The outcomes of this study support and align with existing literature, demonstrating a low rate of surgical site infections, minimal recurrence, and no cases of flap necrosis. In this study, only 8% of patients developed infection of the surgical site, which was successfully managed with oral antibiotics. Additionally, 6% of patients experienced seroma formation, which resolved with stitch removal at the affected site, eliminating the need for further surgical intervention. These results compare favourably to those reported in other studies.

The hospital stay duration, averaging 1.87 ± 0.80 days, was recorded to be lesser than those reported in the previously existing literature. This is a notable advantage, as it helps lower hospitalization costs for patients. The postoperative pain level, assessed using the VAS scale 24 hours after surgery, averaged 3.45, categorizing it as moderate and aligning with findings from earlier research. Notably, no cases of flap necrosis were observed, which compares favourably to other studies.[1,3,5,11,13,16] Recurrence was recorded in only two patients (2%) within a time duration of six months following surgery. The rate of relapse reported here, remains within an acceptable range and is consistent with results from other studies. A contributing factor to recurrence in these cases was poor adherence to postoperative guidelines, particularly the failure to maintain regular hair removal from the nape of the neck. The accumulation of hair in the natal cleft led to reinfection and the formation of a new sinus. Thus, 86% of patients experienced complete primary healing, demonstrating the effectiveness of this procedure in managing primary pilonidal sinus disease of the natal cleft.

Conclusion

The Karydakis flap proved to be an effective and reliable surgical technique for primary pilonidal sinus disease, with 86% of patients achieving complete primary healing without complications. Its design supports faster recovery, minimal postoperative issues, and reduced recurrence, making it a preferred option in clinical practice.

Strengths and Limitations: The follow up time period of one year was a major strength in this study as it allowed for a thorough assessment of complications and recurrence rates. However, a limitation of the study was the lack of comparison between the Limberg flap reconstruction procedure and other flap rotation techniques.

Conflict of Interest: None
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Authors Contribution: All authors are responsible for integrity of the study and had substantial contributions according to ICMJE as follows:

WMC: Literature search, conceptualization of project and writing and revision of manuscript

WA & HA: Data collection and literature search and writing

HA: Data collection and literature search and writing

FT: Literature search, Data collection and writing, revision

RA: Data collection, Statistical analysis revision

SZ: Literature search, analysis and revision of manuscript.

Original Article

Association of Maternal Education and Socioeconomic Status with the Management of Febrile Children Under 10 Years of Age in Lahore

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Abstract

Background: Parents frequently become anxious when dealing with febrile children. Inadequate maternal education and poor awareness can lead to improper management of febrile children which can lead to the prescription of inappropriate medication and other adversities like seizures, convulsions, brain damage, and even death.

Objective: The aim of this study is to assess the association of maternal education and socioeconomic status with their knowledge, attitudes, and practice in managing febrile children under 10 years of age in Lahore.

Methodology: This was a descriptive cross-sectional study held in January and February 2024 conducted amongst parents of children under 10 years of age present at CMH Lahore and The Children's Hospital Lahore.

Results: Our study found 82.2% of parents considered fever to be hazardous to health. 37% defined fever at 38°C. 35.2% of the total participants gave antipyretics as their initial step to manage febrile children. 29.5% of the mothers with complete university education used digital thermometers. Fear of adverse outcomes included dehydration (14.2%), brain damage (9.3%), seizures (32.8%), death (3.6%) while 23.5% considered all of these to be caused by fever.

Conclusion: Maternal education is positively associated with both the use of antipyretics and knowledge about fever. Educated Mothers are more likely to use thermometers and to alternate between different antipyretics. The fear of unfavorable outcomes is common with a belief that fever could lead to adverse effects such as dehydration, confusion, lethargy, seizures, and brain damage.

Keywords: Fever, Antipyretics, Parents, Knowledge, Behavior

Introduction

Febrile children are a common cause of concern for parents. It is one of the most frequent complaints in emergency department visits and antipyretics are the most common medications administered to children. Fever is defined as a core temperature (rectal) of 37.5°C–38.3°C and a skin temperature (axillary) >37.2°C.[1] Fever can be an indicator of benign (e.g., the common cold) or severe conditions (e.g., lethal diseases and meningitis) and is usually self-limiting in children. Fever often accompanies self-limiting viral infections, though, in less than 10% of instances, it might indicate more severe illnesses. It occurs when either endogenous or exogenous pyrogens cause an elevation in the body's thermoregulatory set-point. It can be characterized as low grade [37.3 to 38.0 °C], moderate grade [38.1 to 39.0°C], high grade [39.1 to 41°C] and hyperthermia [>41 °C].[2]

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Most parents seek information about fever management and worry about the potentially severe consequences of fever, such as seizures, brain damage, and even death, although these outcomes are rare, leading to heightened anxiety.[3] Physicians and nurses typically serve as the main sources of guidance on fever management for parents and caregivers. However, there exist differences in perspectives between parents and physicians regarding the use of fever-reducing medications.[4] Pediatricians typically start antipyretic treatment when a child's temperature rises above 38.3°C (101°F), primarily to improve the child's overall comfort.[5] Although only 13% explicitly cite discomfort as the main reason, enhancing comfort is generally understood as a key goal of antipyretic use.[6] Mothers typically identify fever based on their child's overall appearance and often resort to self-medication.[7] Improper management of fever can pose potential harm, with reported adverse effects if not handled appropriately.[8] Providing parents with consistent, evidence-based information on childhood fever management is crucial, and this can be accomplished through educational initiatives on fever and enhanced access to primary care.[9] Approximately 30 percent of Pakistan's population consists of children under 10 years imposing a high burden of childhood illnesses such as fever. There have been, however, limited studies and awareness programs to expand the knowledge of parents in this region. Moreover, a gap in existing studies acts as a hurdle in raising awareness amongst the parents. This study aims to assess the association of parental education and socioeconomic status with their knowledge, attitudes, and practice in managing febrile children under 10 years of age.

Methodology

This was a descriptive, cross-sectional study carried out between January and February 2024 to assess the knowledge and management of fever amongst parents of children under 10 years of age in CMH Lahore and The Children's Hospital Lahore.

Ethical Consideration: Ethical approval (Approval No. ORIC-CMH-LMC-2024 0021, Dated: 01/04/2024) was obtained from the Office of Research, Innovations, and Commercialization (ORIC) CMH Lahore Medical College and IOD, Dated: Data was collected after informed written consent and confidentiality of data was explained. was obtained from the Office of Research, Innovations, and Commercialization (ORIC) CMH Lahore Medical College and IOD. The technique employed was convenience sampling. The sample size was calculated to be 246 with a 95% confidence interval and 6% error margin using the formula n = Z2*P (1-P)/m2). The parameters used were p= 0.36, z= 1.96, e= 0.06. A p-value <0.05 was considered significant. The confidence interval was >95%.[10]

Inclusion Criteria:

The inclusion criteria consisted of mothers of febrile children under 10 years of age presenting in the outpatient department of CMH Lahore and The Children's Hospital Lahore presenting from different areas of Punjab.

Exclusion criteria:

Exclusion criteria was children above 10 years of age, those who were not febrile, and those who had serious medical conditions. The sociodemographic status of the participants was defined as low class (<50,000 rupees), middle class (50,000 to 100,000) and high class (>20,000).[10]

The data was collected through a pre-tested questionnaire conducted in person through verbal communication with parents of children under 10 years of age.[11] Verbal consent was acquired from the participants. The privacy of all participants was respected, and all information obtained was kept confidential. Sociodemographic data (age, origin, socioeconomic level) and data related to knowledge (7 items), behavior (7 items), and fears (6 items) in the management of fever were collected by a questionnaire. The questionnaire was adapted from a published research paper.[11] The value of reliability for the questionnaire was calculated with Cronbach's alpha method (by administering the tool to about 20 parents who were not included in the sample) yielding a value of 0.613. The Author of the questionnaire gave his permission for the usage of the scale in the published research article. Moreover, for validity, the questionnaire was also checked by experts in the field.

Statistical Analysis

The dataset was checked for missing data before analysis. It was then analyzed through Statistical Packaging for the Social Sciences Software (SPSS) version 29. Descriptive analysis was performed in which frequencies, means, and standard deviations were obtained to explain the demographic characteristics of the participants. The data was then represented through charts and tables. Chi-square test was used to check the association of maternal

education with knowledge of fever and antipyretic usage as well as socioeconomic status with use of antipyretics.

Results

A total of 250 mothers were extended invitations to participate in the study, and 247 responded, resulting in a response rate of 98.8%. No case was excluded. Sociodemographic outcome measures are described in Table I. The responses for the knowledge of fever are presented in Table II. Out of all the survey participants, 203 (82.1%) considered that fever was detrimental to health. 166 parents (67.2%) opted to use a thermometer for measuring body temperature, while 79 mothers (32%) abstained from such practice. Most mothers considered a temperature of 39°C to be notably severe. A total of 82 (32.8%) participants held the belief that fever could precipitate seizures, while 58 (23.5%) believed it could lead to seizures, brain damage, or death. Removal of clothing and liquid provision was opted by 37.2% of the respondents as their initial treatment, while 35.2% percent administered antipyretics to their child. 77.3% sought medical advice during their child's recent fever episode. 42.5% practiced routine co-sleeping. 41.3% of the participants anticipated a physical examination from the doctor, while 22.7% expected antipyretic medications. Most of the participants in all three socioeconomic classes used antipyretics preferring acetaminophen and ibuprofen over the others. The use varied from 1 to 6 times a day. The drugs were used after a prescription from the pediatrician by about half of the people. 95% of the respondents used antipyretics, with 47% using acetaminophen, 32% ibuprofen, and 17% both. Table III presents the results for association of maternal education and management of fever. Mothers with higher education were more inclined to use thermometers and opted for alternate use of antipyretics switching between acetaminophen and ibuprofen. Mothers with complete university education showed the highest preference for acetaminophen and ibuprofen while those with complete primary education employed alternate antipyretic therapy. In total, 61% followed alternating antipyretic drug regimens as recommended by pediatricians. In relation to behaviors driven by fear of fever, 55% of parents reported waking their child at night to administer antipyretics, while 43% chose not to disturb their child's sleep.

There was a statistically significant association between socioeconomic status and the use of antipyretics, type of drug used, frequency of administration, and source of indication (Table IV). Lower and middle classes predominantly used acetaminophen or its combination with ibuprofen, while upper classes showed a preference for ibuprofen. Frequency of drug administration varied, with middle and upper classes more likely to use antipyretics 5–6 times/day. Pediatricians were the main source of recommendation, especially in the lower class.

Table I: *Frequency of participants with respective educational and socioeconomic levels*

n = 247		Frequency (%)
Maternal Education	Incomplete primary education	62 (25.1)
	Complete primary education	47 (19)
	Incomplete secondary education	14 (5.7)
	Complete secondary education	39 (15.8)
	Complete university education	83 (33.6%)
	N/A	2 (0.8)
Socioeconomic level	Lower class	100 (40.5)
	Middle class	109 (44.1)
	Upper class	38 (15.4)

n=Number of Participants, Data presented as frequency and percentages.

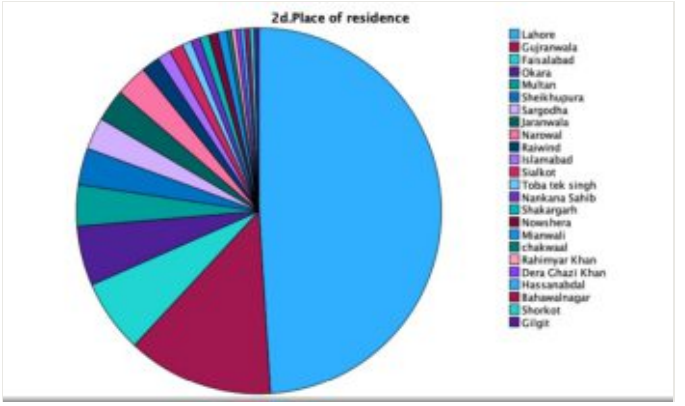

Figure-I: *Place of residence of the study participants*

Table II: *Knowledge of fever among the mothers with their respective frequency.*

n = 247		Frequency (%)
Q3. Do you use a Thermometer to measure body temperature?	Yes	166 (67.2)
	No	79 (32)
Q4. If you use a thermometer, what type is it?	Ear	1 (0.4)
	Forehead	5 (2)
	Digital	73 (29.6)
	Mercury	98 (39.7)
	N/A	70 (28.3)
Q5. If you use a thermometer, in what part of the body do you take the temperature?	Armpit	136 55.1)
	Forehead	12 (4.9)
	Mouth	28 (11.3)
	N/A	71 (28.7)
Q6. If you do not use a thermometer what method do you use?	by hand	78 (31.6)
	flushing and fatigue	6 (2.4)
	N/A	163 (66)
Q7. What temperature do you consider fever (in Celsius)?	37	7 (2.8%)
	37.5	44 (17.8)
	38	84 (34)
	38.5	41 (16.6)
	>39	30 (12.1)
	N/A	41 (16.6)
Q9. Do you think fever may cause any of the following?	Dehydration	35 (14.1)
	None	36 (14.6)
	Brain damage	23 (9.3)
	Seizures	81 (32.8)
	Death	9 (3.6)
	All	58 (23.5)
	Confusion and Weakness	5 (2)

n= Number of Participants, Data is presented as frequency and percentage

Table III: *Association of maternal education and management of fever*

		Which drug(s) do you normally use?					p-value
		Acetaminophen	Ibuprofen	Acetaminophen and ibuprofen	Augmentin	Amoxicillin	
Level of maternal education	Incomplete primary education	29	14	14	1	0	> 0.05
	Complete primary education	26	6	12	0	1	
	Incomplete secondary education	6	3	4	1	0	
	Complete secondary education	18	15	5	0	1	
	Complete university education	36	40	7	0	0	
		How often do you give it to your child?					
		1 to 2 per day	1 to 2 per day	3 to 4 per day	5 to 6 per day		p-value
Level of maternal education	Incomplete primary education	23	32	2	5		
	Complete primary education	14	28	4	1		
	Incomplete secondary education	3	4	4	3		<0.001
	Complete secondary education	5	23	3	8		
	Complete university education	35	32	14	2		
		Do you alternate between several anti-fever drugs?					
		Sometimes	never	Always	N/A		p-value
Level of maternal education	Incomplete primary education	34	21	7	0		
	Complete primary education	24	19	3	1		
	Incomplete secondary education	9	5	0	0		<0.001
	Complete secondary education	22	12	5	0		
	Complete university education	62	18	3	0		

n= Number of Participants p-value calculated by Chi square test and p value < 0.05 considered significant.

Discussion

In our study, the population consisted of mothers of children 10 years, of whom 33.8% had complete university education. The participants were based in different parts of Punjab and comprised more of lower

Table IV: *The association of socioeconomic status with use of antipyretics.*

Socio-economic Status	Do you use any drug to lower the fever?			p-value		
	Yes	No				
Lower class	99	1				
Middle Class	104	5		0.008		
Upper Class	33	5				
Which drug(s) do you usually use?						
	Acetaminophen	Ibuprofen	Acetaminophen and ibuprofen	Augmentin	Amoxicillin	p-value
Lower class	54	16	24	0	1	
Middle class	45	47	14	1	1	0.005
Upper class	17	16	4	1	0	
How often do you give it to your child?						
	1 to 2 per day	3 to 4 per day	5 to 6 per day	N/A	p-value	
Lower class	31	60	5	4		
Middle class	35	45	16	13	0.025	
Upper class	14	16	6	2		
If you do so, who gave you the indication?						
	Family/Friends	Pharmacist	Pediatrician	label	N/A	p-value
Lower class	6	10	62	0	22	
Middle class	19	17	57	2	14	0.041
Upper class	4	8	22	1	3	

n= Number of Participants, p-value calculated by Chi square test and a value < 0.05 is considered significant.

and middle socioeconomic groups. Although recent research suggests a more permissive approach to fever because of its antimicrobial and immune developing function, our results showed that 82.2% of people considered fever to be bad for their health. 67% of the participants used a thermometer to check for fever at home.[12] Despite the hazards of mercury thermometers in cases of mishandling, that include sensory changes, cognitive defects, and incoordination, 39% of the people used them, followed closely by digital thermometers.[13] 28% of the mothers did not use thermometers at all and relied on palpation by hand to determine fever. There was limited knowledge and access to other types such as ear or forehead thermometers despite the ease of usage. The predominant site to check fever was axillary which is considered safe and is recommended by The American Academy of Pediatrics.[14] About 34% of the participants defined fever in children accurately as being >37.5 which is according to UNICEF guidelines.[15] Over two-thirds, however, could not correctly define fever.

The first line of management by 37.2% of mothers was to remove the clothes of febrile children and give them fluids. While 35.2% gave antipyretics which depicts their common use since they are easily available and give rapid relief. Although these should not be given immediately if the temperature is higher than normal, but when the child is in pain, discomfort, or lethargic.[16] The benefits of using physical methods to lower temperature are well-backed scientifically. About 59.2% of the mothers used sponging with lukewarm water to help lower temperature which was found to be more effective than using antipyretics alone.[17] Almost all of the participants got their children checked during recent episodes of fever and

about half made sure that their children slept with them during febrile episodes. This reflects their increased fear of the consequences of fever like in other regions. Most of them considered fever as a cause of seizures, dehydration, brain damage, and death in children which leads to elevated anxiety in dealing with febrile children.[18] Studies have claimed, however, that febrile seizures do not cause brain damage and death in most cases.[16]

During their visit to the pediatrician, mothers preferred a physical examination (41.3%) followed by an indication for antipyretics (22.7%) which shows their awareness about the fact that fever has an underlying cause. Almost all of the participants used drugs to lower fever. Acetaminophen was used abundantly and second in line was Ibuprofen. 61.1% of the mothers gave alternate doses of acetaminophen and ibuprofen which may be more effective in lowering body temperature but not so much in reducing a child's discomfort.[19] A small percentage of people were incorrectly given antibiotics for fever which depicts their lack of knowledge and can lead to adverse effects and multidrug resistance.[20] Almost half of the parents gave the correct dosage of antipyretics but 32.4% underdosed which can cause increased load on health services. Many parents tend to give when there is little to no fever which can mask serious illnesses or in high doses, cause hepatotoxicity.[21] More than half of the total parents woke their sleeping children to give them antipyretics which is not recommended as the aim of treating fever is to minimize discomfort of the child rather than reducing the temperature.[22]

Our research presents a strong correlation between maternal education and the use of thermometers for temperature monitoring [$p<0.05$]. Parents with high maternal education had a significant proclivity to use thermometers. Mothers with limited education had constrained awareness regarding the management of fever. Prior studies have validated that maternal understanding regarding fever management profoundly augments with higher education.[23] Parents frequently used digital thermometers in the armpit for measuring the temperature as they provide accurate, quick results and are cost effective. Given the fluctuation in measurements obtained from various types of thermometers and different measurement sites, the natural variation of body temperature appears erratic. For evaluation and counseling purposes with parents, reference values in literature recommend that a moderate fever is signified by an axillary temperature of 38.5°C which was what most of the educated mothers defined it as.[24]

Parents significantly employed acetaminophen for the treatment of fever. Acetaminophen was extensively utilized as an antipyretic since it is easily available and commonly known to most parents. Furthermore, it has remarkable potency and an excellent safety profile.[25] It reaches peak plasma concentration within 30 minutes of oral intake, with the onset of the highest temperature reduction occurring approximately within 2 hours thereby reducing discomfort in less time.

The results of our study indicate that better-educated parents opted for alternative use of antipyretics whereas those with limited levels of education did not.[25] Studies have shown that alternate use of ibuprofen and acetaminophen is more effective at lowering body temperature but their effect on reducing the discomfort of the child is not well documented.[20] However, studies reporting the safe effective dosage and alternating the use of antipyretics are limited. Most parents of all three socioeconomic classes used antipyretics. Amongst them, most belonging to lower socioeconomic status preferred acetaminophen with ibuprofen second in line (p value= 0.005). This is because of the cost-effectiveness, easy availability, and common use of these medications. Acetaminophen is a safe drug while ibuprofen can cause febrile seizures in a few genetically susceptible people.[16] About half of the parents gave correct dosage while others dose 1-2 times per day which is sub therapeutic for febrile children.[25] Empowering parents with accurate, evidence-based information may reduce the misuse of medications, prevent unnecessary diagnostic testing, and alleviate the anxiety often associated with childhood febrile illnesses.

Conclusion

Maternal education is positively associated with both the use of antipyretics and knowledge about fever. Educated Mothers are more likely to use thermometers and to alternate between different antipyretics. The fear of unfavorable outcomes is common with a belief that fever could lead to adverse effects such as dehydration, confusion, lethargy, seizures, and brain damage.

Limitations and Recmondations: The study was limited to the parents of febrile children in CMH Lahore and The Children's Hospital Lahore so the results may vary in a different setting. Future studies at larger scales are recommended to identify gaps in knowledge and the influence of factors such as education and socioeconomic status. The findings of current study highlight the need for targeted educational programs to train parents across all socioeconomic groups in the appropriate management of fever, including correct medication use, dosing frequency, and seeking professional medical advice.

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Authors Contributions:

The listed authors are responsible for the integrity of the study and have substantially contributed in accordance with the ICMJE guidelines, as detailed below:

ABA: Conceptualizing, Data collection, Results, Drafting, Writing, Editing, Reviewing

MW: Literature review, Data collection, Writing, Reviewing

QUK: Supervising, analysis, Writing, Reviewing

IM: Literature review, Analysis, Results, Editing, Reviewing

EF: Data collection, analysis, editing, reviewing

RM: Literature search, writeup, Data collection, editing, revision

Original Article

Frequency of Pelvic Endometriosis and Serum Prolactin Levels Among Infertile Women at a Tertiary Care Hospital - An Observational Study

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Abstract

Background: Endometriosis, a common benign condition affecting 10–15% of women of reproductive age, is strongly associated with infertility. It is detected in 25–50% of infertile women and 12–32% of those with pelvic pain. Prolactin secretion from endometriotic implants may contribute to ovarian dysfunction and impaired fertility.

Objective: This study aims to determine the frequency of pelvic endometriosis in infertile patients and compare serum prolactin levels among infertile patients with and without endometriosis.

Methodology: It was a cross-sectional study. One hundred and fifty female patients who met the inclusion criteria and presented with complaints of infertility to the outpatient clinic of Jinnah Hospital Lahore were included after informed consent. A 5 mL blood sample was sent to the laboratory for serum prolactin analysis. A consultant radiologist performed transvaginal ultrasound on all patients, for the confirmation of pelvic endometriosis. Mean prolactin levels in females with and without endometriosis were compared using Student's t-test ($p < 0.05$ was considered significant).

Results: The study found that 20.67% (n=31) of infertile female patients who presented to the tertiary care hospital's outpatient department had pelvic endometriosis. When the mean serum prolactin levels of infertile patients with and without endometriosis were compared, the prolactin levels in cases with endometriosis were 22.74±2.03 ng/mL, and in cases without endometriosis were 13.50±2.49 ng/mL, with a p value of 0.0001.

Conclusion: It is concluded that hyperprolactinemia does exist in infertile patients with endometriosis. However, further studies assessing prolactin concentrations across different stages of endometriosis are required to confirm this association.

Keywords: Infertility, Endometriosis, Prolactin, Hyperprolactinemia.

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Introduction

Endometriosis is a benign condition characterized by the presence of endometrial glands and stroma outside the uterine cavity. While lesions are most commonly found in the pelvis,

they can also occur in the intestines, diaphragm, or pleura. Despite being non-malignant, ectopic endometrial tissue often leads to infertility, dysmenorrhea, and dyspareunia due to associated inflammation.[1] It affects approximately 10% of women of reproductive age globally, although prevalence estimates vary by population. Accurate diagnosis is challenging, as many women are asymptomatic or present with nonspecific symptoms, and confirmation typically requires surgical evaluation.[2]

The existence and growth of functioning endometrial glands and stroma outside of the uterine cavity are the hallmarks of endometriosis, a chronic and recurring condition. It causes a wide range of debilitating symptoms and negatively impacts the ability to reproduce. Dysmenorrhea, dyspareunia, infertility, dyschezia, pelvic or lower abdominal pain, irregular bleeding, and persistent exhaustion are among the symptoms.[3] Endometriosis is primarily diagnosed and treated via laparoscopy, which remains the gold standard for both diagnostic confirmation and therapeutic intervention.[2] International studies report a prevalence ranging from 29% to 48.4%, whereas local data, derived from an older retrospective study based on secondary sources, suggest a considerably lower prevalence of 16.8%. While one study demonstrated significantly elevated prolactin levels in women with endometriosis another study found no statistically significant difference between the two groups.[3,4] This discrepancy highlights the need for further well-designed studies to elucidate the potential role of hyperprolactinemia in the pathophysiology of endometriosis.[5]

More recent studies show that prolactin can contribute to the development of endometriosis by sensitizing the nociceptors, which intensifies the pain experienced in the pelvis. Furthermore, research has shown that infertile women with more advanced stages of endometriosis tend to have higher prolactin levels in comparison to women without the disease, which indicates that it may serve as a prognostic biomarker. Still, the differing results fro+m studies emphasize the need to further understand this complex relationship.[6] An infertile woman may have high prolactin levels. Prolactin levels should be low in women who are not nursing or pregnant. A non-pregnant woman may have trouble getting pregnant if her prolactin levels are abnormally high.[7]

Infertility is a distinct medical condition that affects couples and refers to the inability to conceive despite regular, unprotected intercourse. It is defined as failure to achieve pregnancy after 12 months in women under 35 years of age, and after 6 months in women aged 35 or older.[8,9] A study conducted among 518 recently married textile workers in China, aged 20–34 years and actively attempting conception, reported a cumulative pregnancy rate of approximately 50% within two menstrual cycles and 88% within six months. The estimated monthly fecundability ranged between 0.30 and 0.35.[10] Similarly, in a population-based study involving 867 women from the general community engaging in unprotected intercourse, conception rates were 54%, 76%, and 89% within 6, 12, and 24 months, respectively.[11]

There is a lack of research specifically focused on pelvic endometriosis and its association with prolactin, and existing studies show inconsistent findings. This study aims to contribute to the understanding of the local disease burden in our community. As both elevated serum prolactin levels and pelvic endometriosis are associated with infertility, clarifying their relationship may assist gynecologists in providing more effective care. This study aims to determine the frequency of pelvic endometriosis in infertile patients and compare serum prolactin levels among infertile patients with and without endometriosis.

Methodology

This cross-sectional study was conducted at the Gynecology Unit of Jinnah Hospital, Lahore.

Ethical Consideration:

Ethical approval was taken from the institutional review board(Reference No. CPSP/REU/OBG-2016-055-7472, Dated: 23/04/2018). Informed written consent was obtained from the participants, and the confidentiality of their data was clearly explained.

Inclusion criteria:

Infertile female patients between the ages of 18 and 45 who presented to this tertiary care hospital were included. Informed consent was taken from all the participants.

Exclusion Criteria: were as follows: patients with history of more than five prior abdominal surgeries, those with active infections identified by a total leukocyte count (TLC) greater than 11,000 cells/mm³, patients with a pituitary adenoma diagnosed on CT scan, individuals with thyroid dysfunction defined by serum TSH levels less than 0.5 mU/L or greater than 5.7 mU/L, patients diagnosed with pelvic inflammatory disease or polycystic ovarian syndrome based on ultrasound findings and clinical history, and those who had used tranquilizers, dopamine antagonists, or antiemetic medications within the previous three months.

At a 95% confidence level, a sample size of 150 was determined using a non-probability consecutive sampling technique. After obtaining informed consent, 150 female patients who fulfilled the inclusion criteria and presented with infertility complaints at the gynecology outpatient department of Jinnah Hospital, Lahore, were enrolled in the study. Data for all study variables were recorded using a structured Performa. A 5 mL venous blood sample was collected from each participant under aseptic conditions. The samples were transferred to serum vials and sent, along with baseline investigations, to the laboratory at Allama Iqbal Medical College, Lahore, for serum prolactin analysis. Laboratory reports were retrieved on the following day. Additionally, all participants underwent transvaginal ultrasonography performed by a consultant radiologist, for diagnosis of pelvic endometriosis. Strict confidentiality of patient data was maintained throughout the study.

Statistical Analysis: SPSS 17.0 was used to analyze and evaluate the data. Frequencies and percentages are given for categorical variables. Mean and standard deviation is given for continuous variables as data distribution was normal. The mean prolactin level in females with and without endometriosis was compared using the Student's t-test, with a p-value of less than 0.05, which is considered significant.

Results

Table I: *Descriptive characteristics of the study population*

Distribution of age (n=150)		
Age in years	**Number of patients**	**%**
18-30	113	75.33
31-45	37	24.67
Total	150	100
Mean ± SD	27.75 ± 4.76	
Type of infertility (n=150)		
Type of infertility	No. of patients	**%**
Primary	106	70.67
Secondary	44	29.33
Total	150	100
Frequency of pelvic endometriosis among infertile females		
Pelvic Endometriosis	No. of patients	**%**
Yes	31	20.67
No	119	79.33
Total	150	100

n = Number of participants, % = Percentage

In this study a total of 150 cases who met the selection criteria were enrolled. The mean ± SD (standard

Table II: *Comparison of mean serum prolactin levels among infertile patients with and without endometriosis*

	With endometriosis	**Without endometriosis**	**p-value**
Serum prolactin level	Mean ± SD	Mean ± SD	
	22.74 ± 2.03 ng/mL	13.50 ± 2.49 ng/mL	0.0001*

The mean prolactin level in females with and without endometriosis was compared using the Student's t-test. A p value of less than 0.05 is considered significant.

deviation) age was 27.75 ± 4.76 years. Out of total 70.67% (n=106) had primary infertility and 29.33% (n=44) had secondary infertility. The frequency of pelvic endometriosis among infertile females presenting to the outpatient department is 20.6% (31/150 patients). Descriptive features of the study participants are given in table-I.

Table III: *Comparison of serum prolactin level among infertile patients after stratification for age and type of infertility*

Stratification for age (n=150)			
Age in years	Mean ± SD serum prolactin level		p-value
	With endometriosis	Without endometriosis	
18-30	22.96 ± 1.93 ng/mL	13.47 ± 2.45 ng/mL	0.0001*
31-45	21.60 ± 2.41 ng/mL	13.56±2.63 ng/mL	0.0001*
Stratification for type of infertility (n=150)			
Infertility	Mean ± SD serum prolactin level		p-value
	With endometriosis	Without endometriosis	
Primary	23.04±1.99 ng/mL	13.57 ± 2.54 ng/mL	0.0001*
Secondary	21.50±1.87 ng/mL	13.34± 2.41 ng/mL	0.0001*

The mean prolactin level in females with and without endometriosis was compared using the Student's t-test while using stratification for age and type of infertility. A p value of less than 0.05 is considered significant.

A comparison of mean serum prolactin levels in infertile females with and without endometriosis showed significantly higher levels in the endometriosis group (table-II).

Comparison of serum prolactin level in females with and without endometriosis after stratification for age and type of infertility showed significant difference depicted in table-III

Discussion

This study was conducted to determine the prevalence of pelvic endometriosis among infertile female patients and to explore its association with serum prolactin levels. Based on the clinical diagnostic criteria prevalence of endometriosis was found to be 20.67% in the current study. Furthermore, a comparative analysis of serum prolactin levels revealed that women with endometriosis had significantly elevated levels of prolactin (22.74 ± 2.03 ng/mL) compared to those without endometriosis (13.50 ± 2.49 ng/mL). The statistically significant difference observed in prolactin levels suggests an underlying hormonal dysregulation in women with endometriosis. This finding highlights hyperprolactinemia as a potential contributing factor in the disease development or progression. Elevated prolactin may influence reproductive hormone balance, potentially disrupting ovulatory function and endometrial receptivity, thereby playing a role in the infertility commonly associated with endometriosis.[12,13]

When these findings were compared with the global data, they fell within the lower range of reported prevalence rates. International literature indicates that the frequency of endometriosis among women of reproductive age, particularly those experiencing infertility, ranges from 29% to 48.38%.[14] Another study conducted in Ireland reported the prevalence of 37%.[15] However, our results are closely aligned with a regional study conducted in Pakistan, which reported a prevalence of 24% among infertile women.[16] This similarity concurs credibility to our findings and suggests a relatively consistent prevalence rate within the local population across different tertiary care settings. The variation in prevalence across studies could be attributed to differences in study design, diagnostic criteria or sample size. Geographical and demographic differences, such as variations in ethnicity, healthcare access, and awareness levels, may also contribute to the inconsistent prevalence rates observed in the literature.[15]

Along with highlighting the prevalence of endometriosis, our study also found elevated prolactin levels in affected women, which is consistent with previous research findings. For instance, one study demonstrated significantly higher mean prolactin levels in patients with endometriosis

compared to controls (23.02 ± 1.25 ng/mL vs. 17.22 ± 1.22 ng/mL, p=0.004).[17] These findings are in concordance with our results and reinforce the fact that hyperprolactinemia may be more than a coincidental finding in endometriosis. It may, in fact, reflect an underlying pathophysiological mechanism linking hormonal imbalance to the development or exacerbation of endometrial lesions, particularly among women presenting with infertility.[18] Taken together, these findings contribute to the growing body of evidence suggesting that endometriosis is not only underdiagnosed but also potentially influenced by hormonal alterations, including elevated prolactin levels.[18,19] Recognizing this association is important for clinical management, as it opens avenues for targeted hormonal evaluation and therapy in women presenting with unexplained infertility or pelvic pain.

Conclusion

It is concluded through this study that hyperprolactinemia is associated with endometriosis in infertile patients.

Limitations and Recommendations: The generalizability of this study is limited as it is being conducted at a single institution. Further prospective studies with larger sample sizes and multicenter involvement are warranted to validate these findings and explore the clinical implications of hyperprolactinemia in the diagnosis and management of endometriosis.

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Authors Contribution

All the authors made substantial contributions equally in accordance with ICMJE guidelines as mentioned below:

ZA: Conception of the work, interpretation of data, critical review, and final approval of version

AW: Conception of idea of study, reviewing it critically and approving the final version of work

AA: Contribution to the design of the work, Critical review of the work, helped in drafting of work, assisted in interpretation of data, and final approval of work

FN: Contribution to the study: Drafting the work and revising it critically, reviewing data for the study, helped in conceptualization of idea, helped in shaping the final version to be published.

TL: Conception of the work, interpretation of data, helped in critical review, and final approval of version

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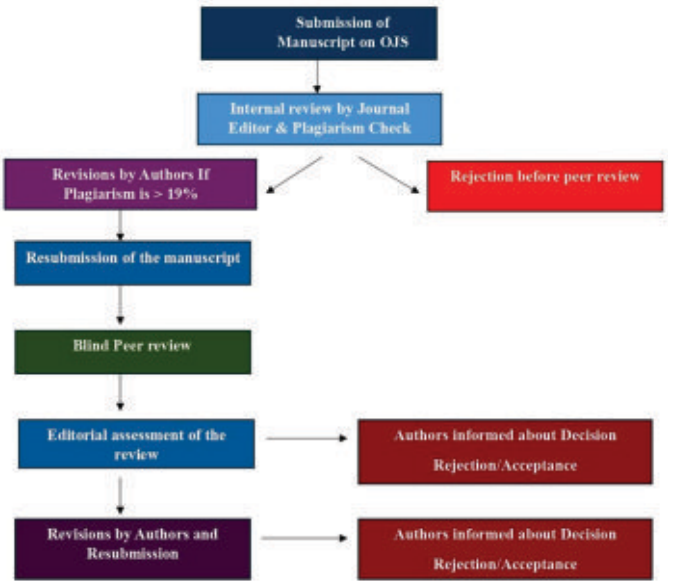

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