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Editorial

Leveraging Artificial Intelligence in Pakistan's Healthcare System: Opportunities and Challenges

Uzma Ahsan

Artificial intelligence (AI) is appearing as a revolutionary tool in healthcare practices, providing possibilities to improve patient management in terms of more efficient diagnosis, treatment plans, and patient assistance and management. In Pakistan, with limited access to the specialized and latest healthcare resources to the majority of the population, the incorporation of AI is expected to meet possibilities as well as challenges. In this editorial, we explore the role of AI in Pakistan's healthcare system, examining its ambit, possible advantages, and the obstacles that must be cleared to recognize and utilize its maximum capacity.

SCOPE OF AI IN PAKISTAN'S HEALTHCARE SYSTEM

AI can revamp and modernize healthcare in Pakistan in numerous domains:

1. Disease Identification and Diagnosis:
For the assistance of physicians various diagnostic and interpretative tools, supported by AI have been established which can analyze medical images, laboratory results, and patient data helping them to precisely diagnose illnesses and foresee their outcomes. By examining multifarious data arrangements, AI algorithms can recognize indirect signs and configurations that may not be obvious to human observers, thereby permitting early discovery of diseases and refining predictive validity.[1]

2. Individual Treatment Planning:
The utilization of AI algorithms has revolutionized patient data analysis, along with genetic info and medical history, to modify treatment plans and augment therapeutic outcomes.[1]

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3. Distant Monitoring and Telemedicine:
Artificial intelligence-backed surveillance equipment and telehealth electronic consultation platforms permit patient monitoring in far-flung areas, thus not only assisting in the early identification of health issues but also allowing well-timed interventions, predominantly in rural and underserved areas.[2]

4. Drug Discovery and Development:
Artificial intelligence systems have the potential to speed up the drug design and development process by scrutinizing massive data collections, foreseeing drug interactions, and recognizing probable recipients for innovative treatments.

5. Healthcare Administration:
Artificial intelligence-supported automated systems can simplify managerial responsibilities, enhance resource distribution, and improve productivity in healthcare facilities.[3]

CHALLENGES OF AI IMPLEMENTATION IN PAKISTAN

The healthcare system in Pakistan is challenged with major hurdles of restricted resources, along with uneven dissemination of healthcare facilities. Additionally, there is a deficiency of qualified and trained physicians. Incorporation of AI in healthcare can provide a possibility to surmount these obstacles and improve healthcare outcomes. Utilization of the latest AI innovations, like machine learning and natural language processing, can not only be helpful in evaluating huge volumes of medical data, but will additionally provide a benefit of facilitating diagnosis, predicting disease outcomes, and modifying treatment plans. Through process automation, AI can also lessen the burden on healthcare professionals and improve efficacy in the healthcare delivery system.
Regardless of its potential benefits, the pervasive implementation of AI in Pakistan's healthcare system faces numerous trials:

1. Data Confidentiality:
For ethical and quality assurance purposes**,** safeguarding the confidentiality and security of patient statistics and documents is of supreme importance. This necessitates the need of implementing vigorous data safety procedures and adherence to regulatory guidelines.[4]

2. Legislative Systems:
The lack of implementation of regulatory regimes for AI-backed medical devices, processes, and telemedicine platforms poses a major challenge for the smooth functioning and implementation of various AI systems in the country.[4]

3. Limited Infrastructure and Resources:
Insufficient substructure, including internet connectivity, and a scarcity of skilled professionals delay the organization and preservation of AI systems in healthcare settings.

4. Ethical Contemplations:
Tackling ethical concerns connected to AI, such as partiality in algorithms, clearness, and liability, is critical to preserve public trust and ensure unbiased healthcare delivery.[5]

5. Accessibility and Impartiality:
Linking the technology gap and guaranteeing impartial access to AI-enabled healthcare services is necessary to avoid broadening inequalities in healthcare access.[6]

CONCLUSION

Artificial intelligence embraces enormous potential for transforming Pakistan's healthcare system, presenting opportunities to augment diagnosis, treatment, and patient care. However, grasping the full potential of AI in healthcare requires addressing challenges related to data confidentiality, supervisory frameworks, substructure, moral principles, and availability. By promoting cooperation among shareholders, investing in infrastructure and training, and developing vigorous regulatory frameworks, Pakistan can utilize the power of AI to improve health outcomes and advance healthcare delivery for its population.

REFERENCES

1. Rajpurkar P, Chen E, Banerjee O, Topol EJ. AI in health and medicine. Nat Med. 2022; 28(1):31-8. doi:10.1038/s41591-021-01614-0.

2. Mahdi SS, Allana R, Battineni G, Khalid T, Agha D, Khawaja M, et al. The promise of telemedicine in Pakistan: a systematic review. Health Sci Rep. 2022; 5(1):e438. doi:10.1002/hsr2.438.

3. Umer L, Khan MH, Ayaz Y. Transforming healthcare with artificial intelligence in Pakistan: a comprehensive overview. Pak Armed Forces Med J. 2023; 73(4): 955-63. doi:10.51253/pafmj.v73i4.10852.

4. Cartolovni A, Tomicic A, Lazic Mosler E. Ethical, legal, and social considerations of AI-based medical decision-support tools: a scoping review. Int J Med Inform. 2022; 161:104738. doi:10.1016/j.ijmedinf.2022.104738.

5. Naik N, Hameed BMZ, Shetty DK, Swain D, Shah M, Paul R, et al. Legal and ethical consideration in artificial intelligence in healthcare: who takes responsibility? Front Surg. 2022; 9:862322. doi:10.3389/fsurg.2022.862322.

6. Ahmed Z, Bhinder KK, Tariq A, Tahir MJ, Mehmood Q, Tabassum MS, et al. Knowledge, attitude, and practice of artificial intelligence among doctors and medical students in Pakistan: a cross-sectional online survey. Ann Med Surg (Lond). 2022; 76:103493. doi:10.1016/j.amsu.2022.103493.

Original Article

Comparison of Patelloplasty versus Patellar Resurfacing in Total Knee Replacement

Farooq Azam Khan, Bilal Ahmad Abbas, Waqas Ali, Talha Qureshi, Kashif Jamal

ABSTRACT

Objective: To compare the effectiveness of patelloplasty versus patellar resurfacing in improving the American Knee Society Score (AKSS) and Oxford Knee Score (OKS) in patients undergoing total knee replacement (TKR).

Methodology: This quasi-experimental study was carried out at the Department of Orthopedics, Sharif Medical City Hospital, Lahore from May 2023 to January 2024. The study approval was taken from the ethical committee of the institution. Using non-probability convenient sampling technique, 60 patients with grade IV knee osteoarthritis for more than six months were enrolled. Two groups of patients were made (30 patients in each group). Patients in group I underwent TKR with patellar resurfacing, whereas patients in group II underwent TKR with patelloplasty. The patients provided written informed consent. The AKSS (clinical and functional) and OKS scores were estimated before surgery, three months, and six months after TKR. The Statistical Package for the Social Sciences (SPSS) version 25 was used to analyze the data.

Results: Preoperative and postoperative AKSS clinical score, AKSS functional score, and OKS score showed statistically significant improvements in both groups (p-value=0.001). However, there was no discernible difference between the patellar resurfacing and patelloplasty groups in preoperative and postoperative AKSS clinical, AKSS functional, and OKS scores (p-value >0.05).

Conclusion: There is no difference in the clinical and functional outcomes of patients who undergo total knee replacement with patellar resurfacing or patelloplasty. Patelloplasty is a safe and equally effective treatment strategy with a decreased incidence of postoperative complications and provides the option of secondary patellar remodeling in case of persistent anterior knee pain.

Keywords: *Total knee replacement. Postoperative complications. Osteoarthritis.*

INTRODUCTION

Osteoarthritis (OA) is the most frequent disorder of joints and fourth major cause of disability worldwide.[1] Its global prevalence rose in the last thirty years from 247.51 to 527.81 million.[2] Around 9.6% increase in years lived with disability (YLD) is attributed to osteoarthritis from 1990 to 2017.[3] It has become a major health challenge leading to pain, disability, loss of function, and financial burden. The most commonly affected joint is the knee joint, responsible for 83% of the cases of osteoarthritis.[1,4] Osteoarthritis has a female predominance and the age group most affected is the elderly between the age of 60 and 70 years.[5]

Total knee replacement has revolutionized the treatment of osteoarthritis. Unfortunately, advanced knee arthritis has no effective treatment option other than surgery. For advanced knee osteoarthritis, the most common and effective surgery with long-term patient benefits is total knee replacement. It has a high success rate.[6] Arthritis is mostly tri-compartmental involving patello-femoral and tibio-femoral compartments. Traditionally, during TKR all three compartments are addressed. Various strategies used in TKR are either patellar resurfacing, selective resurfacing or no resurfacing (patelloplasty).[7] Controversy exists regarding the best strategy to be used during the procedure. The choice of strategy depends on the preference, training, and personal experience of the surgeon. The global data shows various strategies being used by surgeons across the world. The most common complication after TKR leading to dissatisfaction of patients is anterior knee pain in 5-47% of the patients after TKR without resurfacing. To combat the issue, patellar resurfacing was started in TKR but it also has many complications such as tendon rupture, patellar cluck, subluxation, dislocation, loosening, and patellar fracture.[8] More recent trends show a tilt towards more conservative patelloplasty. Patelloplasty has the advantage of conservation of bone stalk and decreased risk of postoperative complications.[7]

The prevalence of osteoarthritis is high in low-income and lower-middle-income countries. The best treatment for osteoarthritis is total knee replacement.[1] There is still controversy regarding the strategy to be used in total knee replacement. To date, there are no local studies or exact guidelines to compare these procedures. In this study, the AKSS and OKS of patients who underwent total knee replacement were compared to determine the effectiveness of patelloplasty and patellar resurfacing in TKR.

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METHODOLOGY

This quasi-experimental study was carried out at the Department of Orthopedics, Sharif Medical City Hospital, Lahore from May 2023 to January 2024. The study approval was taken from the ethical committee of the institution (Letter No. SMDC/SMRC/307-23, 02-04-2023). Using non-probability convenient sampling technique, 60 patients with grade IV knee osteoarthritis for more than six months were enrolled. Two groups of patients were made. Each group had 30 patients. Patients in both groups were matched for age, gender, and body mass index (BMI). Patients in group I underwent TKR with patellar resurfacing, whereas patients in group II underwent TKR with patelloplasty. In patellar resurfacing the patellar articular surface is resurfaced and cut leaving the raw bone. Polyethylene patellar buttons are then attached using bone cement.

In patelloplasty the patellar bone is not resurfaced however all the osteophytes are removed and furthermore the articular area is smoothed with the help of a bone filer.[8] Surgery was performed by the same orthopedic surgeon. The patients provided informed written consent. The team member who was not involved in surgical planning estimated the AKSS and OKS scores before surgery, three months, and six months after TKR. Demographic variables of the study participants like age, gender, and BMI were noted on a proforma.

The AKSS score has two sections: clinical and functional scores with a total score of 100 for each section (Table 1).[9]

The Oxford Knee Score comprises of 12 questions related to pain and how it affects the daily life activities of the patient. Each question is graded from 1 to 5, with the best grade of 1 and the worst grade of 5. The score ranges from 0-60. The lower the score, the better the grade.[10]

STATISTICAL ANALYSIS

The Statistical Package for the Social Sciences (SPSS) version 25 was used to analyze the data. The mean±SD was used to express the numerical variables including age, AKSS, and OKS scores. The qualitative variables such as gender, AKSS, and OKS score grades were represented as frequency and percentage. The AKSS and OKS scores were compared preoperatively and at 6 months follow-up using a paired t-test. The preoperative and postoperative AKSS and OKS scores between the patellar resurfacing and patelloplasty groups were compared using an Independent t-test. The postoperative AKSS and OKS score grades were compared between the two groups by Chi-square test. A p-value of ≤0.05 was taken as significant.

RESULTS

The mean age of the patients was 64.9±3.50 years with an age range of 51-80 years. The majority of the patients 47(78.33%) had an age ranging from 61-70 years, 9(15%) were in the 51-60 years range, and 4(6.67%) in the 71-80 years range. Thirty nine (65%) out of 60 patients were females and 21(35%) were males. The mean body mass index (BMI) of the patients was 28.12±1.43 kg/m^2. No significant difference regarding age, gender, and BMI was found in the two groups (Table 2).

Table 3 shows the preoperative and postoperative scores of study groups. The preoperative and postoperative AKSS clinical, AKSS functional, and OKS scores did not significantly change between the two groups (p-value >0.05). Preoperative and postoperative AKSS clinical score, AKSS functional score, and OKS score showed statistically significant improvements after surgery (p-value=0.001) (Table 4).

Table 1: AKSS Clinical and Functional Score[9]

AKSS Score	Component	Interpretation
AKSS Clinical Score	Pain	Excellent: 80-100 Good: 70-79 Fair: 60-69 Poor: <60
	Range of Motion	
	Anteroposterior Stability	
	Mediolateral Stability	
	Flexion Contracture	
	Extension Deficit	
	Alignment	
AKSS Functional Score	Distance Walked	
	Stairs	
	Use of Walking Aids	

The preoperative AKSS clinical score was poor in all patients. At 3 months of follow-up, 7(23.33%) patients had excellent, 19(63.33%) patients had good, and 4(13.34%) patients had fair score in the patellar resurfacing group, whereas in the patelloplasty group, 7(23.33%) patients had excellent, 17(56.67%) patients had good, and 6(20%) patients had fair score (p-value=0.729). At 6 months, 23(76.67%) patients had excellent and 7(23.33%) patients had good scores in the patellar resurfacing group. In the patelloplasty group, 24(80%) patients had excellent and 6(20%) patients had good scores (p-value=0.733).

The preoperative functional score was also poor in all patients before TKR. At 3 months, 4(13.34%) & 10(33.33%) patients had good scores, 24(80%) & 13(43.34%) patients had fair scores, and 2(6.66%) & 7(23.33%) patients had poor scores in patellar resurfacing and patelloplasty groups, respectively (p-value=0.032). At 6 months, 6(20%) patients had excellent, 17(56.67%) patients had good, and 7(23.33%) patients had fair scores in patellar resurfacing group. Nine (30%) patients had excellent, 14(46.67%) had good, and 7(23.33%) had fair scores in the patelloplasty group (p-value=0.784) (Table 5).

DISCUSSION

Osteoarthritis can be effectively treated with total knee replacement. But some patients experience anterior knee pain after total knee replacement. Patellar resurfacing in TKR was introduced to reduce the likelihood of postoperative knee pain.[11] However, patellar resurfacing was not linked to a significant reduction in anterior knee pain as per a study by Benazzo et al. Instead, it caused an increased incidence of intra-operative fractures and revision surgery.[12]

Table 2: Demographic Variables of the Study Participants

Demographic Variables		Patellar Resurfacing Group	Patelloplasty Group	p-value
Age (Years)	**Mean±SD**	65.60±2.88	64.20±3.96	0.160
Gender (Frequency & Percentage)	**Females**	18(60%)	21(70%)	0.556
	Males	12(40%)	9(30%)	
BMI (kg/m^2)	**Mean±SD**	27.76±1.41	28.47±1.38	0.08

Table 3: Comparison of Mean Preoperative and Postoperative AKSS & OKS Scores between the Study Groups

Knee Scores		Patellar Resurfacing Group	Patelloplasty Group	p-value
AKSS Clinical Score	**Preoperative**	28.24±5.23	28.32±4.85	0.956
	Postoperative at 3 Months	74.96±4.12	73.72±5.17	0.354
	Postoperative at 6 Months	83.28±4.25	82.20±3.86	0.352
AKSS Functional Score	**Preoperative**	48.32±5.02	47.68±5.62	0.673
	Postoperative at 3 Months	63.76±3.98	64.16±5.57	0.772
	Postoperative at 6 Months	73.52±5.45	74.64±5.96	0.492
OKS Score	**Preoperative**	33.92±6.28	32.80±7.15	0.559
	Postoperative at 3 Months	25.36±4.59	23.60±5.46	0.224
	Postoperative at 6 Months	20.32±4.10	19.24±4.67	0.389

Table 4: Comparison of Mean Preoperative and 6 Months Postoperative AKSS & OKS Scores of the Study Group

Knee Scores	Study Groups	Preoperative	Postoperative at 6 Months	p-value
AKSS Clinical Score	**Patellar Resurfacing Group**	28.24±5.23	83.28±4.25	0.001*
	Patelloplasty Group	28.32±4.85	82.20±3.86	0.001*
AKSS Functional Score	**Patellar Resurfacing Group**	48.32±5.02	73.52±5.45	0.001*
	Patelloplasty Group	47.68±5.62	74.64±5.96	0.001*
OKS Score	**Patellar Resurfacing Group**	33.92±6.28	20.32±4.10	0.001*
	Patelloplasty Group	32.80±7.15	19.24±4.67	0.001*

**Significant p-value*

Table 5: Postoperative AKSS Clinical and Functional Score Grading

AKSS Score Grade		Patellar Resurfacing Group	Patelloplasty Group	Chi-Square Statistics	p-value
AKSS Clinical Score Grade	**At 3 Months Follow-up**				
	Excellent	7(23.33%)	7(23.33%)	0.633	0.729
	Good	19(63.33%)	17(56.67%)		
	Fair	4(13.34%)	6(20%)		
	Poor	0(0%)	0(0%)		
	Total	30(100%)	30(100%)		
	At 6 Months Follow-up				
	Excellent	23(76.67%)	24(80%)	0.117	0.733
	Good	7(23.33%)	6(20%)		
	Fair	0(0%)	0(0%)		
	Poor	0(0%)	0(0%)		
	Total	30(100%)	30(100%)		
AKSS Functional Score Grade	**At 3 Months Follow-up**				
	Excellent	0(0%)	0(0%)	6.88	0.032*
	Good	4(13.34%)	10(33.33%)		
	Fair	24(80%)	13(43.34%)		
	Poor	2(6.66%)	7(23.33%)		
	Total	30(100%)	30(100%)		
	At 6 Months Follow-up				
	Excellent	6(20%)	9(30%)	0.48	0.784
	Good	17(56.67%)	14(46.67%)		
	Fair	7(23.33%)	7(23.33%)		
	Poor	0(0%)	0(0%)		
	Total	30(100%)	30(100%)		

**Significant p-value*

The patients in our study had a mean age of 64.9±3.50 years. Patients in an Indian study had an average age of 64.7±5.7 years.[13] The mean age was 63.44 years in another study.[14] In our study, 65% of the participants were females. Noh et al. also reported that 89.2% of the patients were females.[15] All the patients in our study were overweight or obese with a mean BMI of 28.12±1.43 kg/m^2. This is similar to another study in which patients had a mean BMI of 28.16±3.87 kg/m^2.[16] The follow-up period was 6 months in our study. The follow-up duration was 19 months and 3 years in two other studies, respectively.[13,17]

In our study, the mean preoperative AKSS clinical scores were 28.24±5.23 and 28.32±4.85 in patellar resurfacing and patelloplasty patients, respectively with an insignificant difference (p-value=0.956). Moreover, the mean preoperative AKSS functional scores were 48.32±5.02 and 47.68±5.62 in patellar resurfacing and patelloplasty patients, respectively. Another study showed a mean preoperative clinical score of 39 in patellar resurfacing and 38.6 in patelloplasty patients. The mean preoperative AKSS functional scores were 56.25 and 55.75 in patients with patellar resurfacing and patelloplasty, respectively.[16]

Our results showed an insignificant difference in postoperative AKSS scores between patellar resurfacing and patelloplasty groups. The mean postoperative AKSS clinical score at 6 months was 83.28±4.25 in the patellar resurfacing group and 82.20±3.86 in the patelloplasty group, with an insignificant p-value (p-value=0.352). Morrah et al. reported a mean postoperative AKSS score of 94.70 in patellar resurfacing and 98 in patelloplasty patients with no significant difference.[16] In a study by Agarwala et al., postoperative AKSS clinical score in patellar resurfacing and patelloplasty patients was 49 and 48, respectively which was statistically insignificant.[13] The mean postoperative AKSS functional score at 6 months was 73.52±5.45 in patellar resurfacing and 74.64±5.96 in patelloplasty patients in our study. In another study, the mean postoperative functional scores were 76 and 74.75 in patellar resurfacing and patelloplasty patients, respectively. The results were statistically insignificant.[16] The mean AKSS functional scores were 33.67 and 34.93 in resurfacing and patelloplasty patients, with an insignificant difference in a study by Agarwala et al.[13]

In our study, the mean preoperative OKS scores were 33.92±6.28 and 32.80±7.15 in patellar

resurfacing and patelloplasty patients, respectively. The mean 6 month postoperative OKS score was 20.32±4.10 in patellar resurfacing and 19.24±4.67 in the patelloplasty group. In another study, the mean preoperative OKS score was 37 in both groups. The mean postoperative OKS scores were 17 and 18 in patellar resurfacing and patelloplasty patients. The results were statistically insignificant.[17]

Patients who underwent TKR with patellar resurfacing and patelloplasty did not significantly differ in their AKSS scores, according to Agarwala et al., Noh et al., and Kedia.[13,15,18] In a different study, the postoperative AKSS and OKS scores of the two groups did not differ significantly.[17] In contrast, a study conducted in Columbia reported a significant difference in AKSS clinical & functional scores and OKS score, with a much improved score in the patellar resurfacing group.[19] The results of the meta-analysis found that patellar resurfacing resulted in an increase in AKSS clinical and functional scores but had no effect on OKS score.[20] Another study revealed a significant improvement in postoperative AKSS clinical score with patellar resurfacing as compared to patelloplasty. But the difference was insignificant for postoperative AKSS functional score.[14]

CONCLUSION

There is no difference in the clinical and functional outcomes of patients who undergo total knee replacement with patellar resurfacing or patelloplasty. Patelloplasty is a safe and equally effective treatment strategy with a decreased incidence of postoperative complications and provides the option of secondary patellar remodeling in case of persistent anterior knee pain.

LIMITATIONS & RECOMMENDATIONS

The follow-up period was 6 months. Future research should be conducted with a longer follow-up of the patients.

Conflict of Interest: None.

Source of Funding: None.

Authors' Contributions:

F.A.K: Study design & drafting
B.A.A: Literature & drafting
W.A: Data analysis
T.Q: Data correlation
K.J: Proof reading and final approval

REFERENCES

1. Spitaels D, Mamouris P, Vaes B, Smeets M, Luyten F, Hermens R, et al. Epidemiology of knee osteoarthritis in general practice: a registry-based study. BMJ Open. 2020; 10(1):e031734. doi:10.1136/bmjopen-2019-031734.

2. Long H, Liu Q, Yin H, Wang K, Diao N, Zhang Y, et al. Prevalence trends of site-specific osteoarthritis from 1990 to 2019: findings from the global burden of disease study 2019. Arthritis Rheumatol. 2022; 74(7):1172-83. doi:10.1002/art.42089.

3. Zhakhina G, Gusmanov A, Sakko Y, Yerdessov S, Semenova Y, Saginova D, et al. The regional burden and disability-adjusted life years of knee osteoarthritis in Kazakhstan 2014-2020. Biomedicines. 2023; 11(1):216. doi:10.3390/biomedicines11010216.

4. Hamood R, Tirosh M, Fallach N, Chodick G, Eisenberg E, Lubovsky O. Prevalence and incidence of osteoarthritis: a population-based retrospective cohort study. J Clin Med. 2021; 10(18):4282. doi:10.3390/jcm10184282.

5. Vitaloni M, Botto-van Bemden A, Sciortino Contreras RM, Scotton D, Bibas M, Quintero M, et al. Global management of patients with knee osteoarthritis begins with quality of life assessment: a systematic review. BMC Musculoskelet Disord. 2019; 20(1):493. doi:10.1186/s12891-019-2895-3.

6. Adam R, Moldovan C, Tudorache S, Harsovescu T, Orban C, Pogarasteanu M, et al. Patellar resurfacing in total knee arthroplasty, a never-ending controversy; case report and literature review. Diagnostics (Basel). 2023; 13(3):383. doi:10.3390/diagnostics13030383.

7. Uivaraseanu B, Vesa CM, Tit DM, Abid A, Maghiar O, Maghiar TA, et al. Therapeutic approaches in the management of knee osteoarthritis (review). Exp Ther Med. 2022; 23(5):328. doi:10.3892/etm.2022.11257.

8. McConaghy K, Derr T, Molloy RM, Klika AK, Kurtz S, Piuzzi NS. Patellar management during total knee arthroplasty: a review. EFORT Open Rev. 2021; 6(10):861-71. doi:10.1302/2058-5241.6.200156.

9. Iqbal J, Khan A, Rafe-ullah, Khattak AU, Khattak S, Shah FA. Clinical and functional outcome of total knee replacement in osteoarthritic knee. J Liaquat Uni Med Health Sci. 2023; 22(04):225-8. doi:10.22442/jlumhs. 2023.01086.

10. Tay ML, Monk AP, Frampton CM, Hooper GJ, Young SW. The strongest Oxford Knee Score predictors of subsequent revision are "overall pain," "limping when walking," and "knee giving way". J Arthroplasty. 2023; 38(7 Suppl 2):S156-61.e3. doi:10.1016/j.arth.2023.03.001.

11. Grela M, Barrett M, Kunutsor SK, Blom AW, Whitehouse MR, Matharu GS. Clinical effectiveness of patellar resurfacing, no resurfacing and selective resurfacing in primary total knee replacement: systematic review and meta-analysis of interventional and observational evidence. BMC Musculoskelet Disord. 2022; 23(1):932. doi:10.1186/ s12891-022-05877-7.

12. Benazzo F, Perticarini L, Jannelli E, Ivone A, Ghiara M, Rossi SMP. Controversy: supporting patellar resurfacing in total knee arthroplasty - do it. EFORT Open Rev. 2020; 5(11):785-92. doi:10.1302/2058-5241.5.190075.

13. Agarwala S, Shetty V, Karumuri LK, Vijayvargiya M. Patellar resurfacing versus nonresurfacing with patellaplasty in total knee arthroplasty. Indian J Orthop. 2018; 52(4):393-8. doi:10.4103/ortho.IJOrtho_512_16.

14. Siddiqui MS, Parsurampuriya VK, Kumar N, Kumar S. Outcome after total knee arthroplasty with or without patellar resurfacing. Int J Res Orthop. 2021; 7(4):732-8. doi:10.18203/issn.2455-4510.IntJResOrthop20212363.

15. Noh JH, Kim NY, Song KI. Comparison of clinical outcomes between patellar resurfacing and patellar non-resurfacing in cruciate retaining total knee arthroplasty. J Orthop Surg (Hong Kong). 2022; 30(1):10225536221092223. doi:10.1177/10225536221092223.

16. Morrah AN, Elgeidy IT, Mohammed MM, Yassin MA, Ibrahim AA, El Sayed FEM. Patellar resurfacing compared with no resurfacing in total knee arthroplasty. Med J Cairo Univ. 2022; 90(6):1855-65. doi:10.21608/MJCU.2022.272757.

17. Aunan E, Naess G, Clarke-Jenssen J, Sandvik L, Kibsgard TJ. Patellar resurfacing in total knee arthroplasty: functional outcome differs with different outcome scores: a randomized, double-blind study of 129 knees with 3 years of follow-up. Acta Orthop. 2016; 87(2):158-64. doi:10.3109/17453674.2015.1111075.

18. Kedia A. Patelloplasty or patella resurfacing? Answer to anterior knee pain after total knee replacement in Indian patients. Int J Orthop Sci. 2022; 8(4):44-6. doi:10.22271/ortho.2022.v8.i4a.3240.

19. Martinez S, Ron-Translateur T, Cantor E, Palacio JC. Patellar resurfacing in primary total knee replacement: a comparative study at two years of follow-up. Rev Asoc Argent Ortop Traumatol. 2022; 87(6):798-803. doi:10.15417/issn.1852-7434.2022.87.6.1453.

20. Chen K, Dai X, Li L, Chen Z, Cui H, Lv S. Patellar resurfacing versus nonresurfacing in total knee arthroplasty: an updated meta-analysis of randomized controlled trials. J Orthop Surg Res. 2021; 16(1):83. doi:10.1186/s13018-020-02185-5.

Original Article

Association of Early Rise of High-Sensitivity Cardiac Troponin I with Severity of Coronary Artery Disease in non-ST Elevation Myocardial Infarction Patients

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ABSTRACT

Objective: To determine the association of early rise of high-sensitivity cardiac troponin I (hs-cTnI) with the severity of coronary artery disease in non-ST elevation myocardial infarction (NSTEMI) patients.

Methodology: This cross-sectional study was conducted at the Cardiology Department, Fauji Foundation Hospital, Rawalpindi from June to November 2023. After obtaining informed written consent, 100 patients with NSTEMI presenting in the Emergency Department were enrolled using non-probability convenient sampling technique. Patients presenting with the signs and symptoms of coronary artery disease for at least 1 hour were preceded for electrocardiogram (ECG) and high-sensitivity cardiac troponin I levels. After initial management, the patients underwent coronary angiography either by trans-femoral or trans-radial approach. Severity of oronary artery disease was determined by SYNergy between percutaneous with TAXus and cardiac surgery (SYNTAX) score. The association of disease severity as determined by the SYNTAX score was seen with the hs-cTnI levels. Data was analyzed using Statistical Package for the Social Sciences (SPSS) version 25.

Results: The majority of the patients (50%) had SYNTAX score of 0-22 and 35% had score of 23-32. Only 15% of the patients had a SYNTAX score >33. A significant relation was found between the SYNTAX score and hs-cTnI. The level of high-sensitivity troponin I was increased significantly in patients with triple vessel disease.

Conclusion: High-sensitivity cardiac troponin I is a reliable marker of disease severity. A significant association exists between the severity of the disease as indicated by the SYNTAX score and levels of hs-troponin I in patients with NSTEMI. Patients with triple vessel disease are more likely to have higher hs-cardiac troponin I levels.

Keywords: *Coronary artery disease. Troponin I. Non-ST elevation myocardial infarction.*

INTRODUCTION

Coronary artery disease (CAD) is the most common among cardiovascular diseases (CVD), responsible for premature mortality. There is a 42% increase in trends of mortality from CVD since 1990. It also contributes to 180 million disability-adjusted life years.[1] Prevalence of coronary artery disease is high in Nepal, India, Afghanistan, Pakistan, Bhutan, Sri Lanka, Maldives, and Bangladesh. Coronary artery disease is classified into unstable angina, ST-elevation myocardial infarction (STEMI), and non-ST-elevation myocardial infarction. Around 70% of the cases of CAD are caused by NSTEMI. The underlying pathogenesis of NSTEMI involves the disruption of the balance between oxygen supply and cardiac oxygen requirement.[2] The chances of CAD are higher in advanced age, being a significant contributor to mortality. But nowadays, it also affects a considerable proportion of young individuals. The other predisposing factors are high blood pressure, diabetes mellitus, hypertension, deranged lipid profile, overweight, smoking, and positive family history of ischemic heart disease.[3]

Myocardial infarction is characterized by a typical clinical picture, ECG changes, and a rise in cardiac troponin >99th percentile of the upper limit.[4] Cardiac troponin (cTn) is present within the contractile apparatus of myocardial cells and after injury to the myocardium, it is released into the blood. Raised cardiac troponin is the key diagnostic modality for CAD. It has two types: cardiac troponin T (cTnT) and cardiac troponin I (cTnI). But it is also raised in some other diseases such as sepsis & adrenal insufficiency. The majority of the immunoassays available for cTn lack analytical sensitivity resulting in failure to detect cTn during the early phase of NSTEMI and in small infarcts. A relatively new type of troponin known as high-sensitivity cardiac troponin I is now being used due to its high sensitivity. It can measure 5-10 times lower concentration of cTnI.[5] It has been reported that hs-cTnI is more sensitive as compared to hs-cTnT in CAD.[6]

Various scores are implied to assess the extent of the disease and its severity. Some scores also guide about the best treatment option on the basis of angiographic findings. They can also be used as a prognostic factor to monitor the disease.[7] The SYNTAX score is a well-known aid used by cardiologists to assess the severity and extent of CAD. It is also a validated predictor of cardiovascular outcomes.[8]

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This study was done to determine the severity of coronary artery disease using the SYNTAX score in NSTEMI patients and see the association of levels of hs-cTnI with disease severity based on the SYNTAX score. This study will help in risk stratification and early recognition of patients with severe disease so that such patients can be referred for timely therapeutic intervention. It will also have clinical implications in disease prognosis and can be used to monitor for the occurrence of adverse outcomes.

METHODOLOGY

This cross-sectional study was conducted at the Cardiology Department, Fauji Foundation Hospital, Rawalpindi from June to November 2023. The study was approved by the ethical committee of the institution (Letter No. 748/RC/FFH/RWP, 02-05-2023). One hundred patients with NSTEMI presenting in the Emergency Department for at least 1 hour were enrolled regardless of their age or gender. Informed written consent was taken. The patients with unstable angina or STEMI were excluded. Sample size of 100 was calculated at 95% confidence interval with 9% margin of error using the prevalence of NSTEMI as 22.8% by the World Health Organization (WHO) sample size calculation.[9] Patients with typical clinical manifestations of CAD were preceded by ECG and hs-cTnI levels. The patient's age, gender, co-morbids, type of disease, etc. were noted on the proforma. After initial management, the patients underwent coronary angiography either by trans-femoral or trans-radial approach. The SYNTAX score of the patients was also estimated to determine disease severity. The higher the score, the more the severity of the disease.

The SYNTAX score estimates the severity and complexity of CAD on the basis of angiographic findings. It is calculated by adding points assigned to individual lesions with >50% stenosis in vessels with a caliber of >1.5 mm. It ranges from 0 to greater than 60. The SYNTAX score is divided into 3 categories; low: ≤22, intermediate: 23-32, and high: ≥33.[10] The blood samples of patients were sent to the laboratory and hs-cardiac troponin I was estimated using the kit manufactured by Abbot Laboratories. The limit of detection of the kit was 1.2 ng/L. The upper limit used as a reference was 34 ng/L in males and 16 ng/L in females.[11] The association of disease severity as determined by the SYNTAX score was seen with the hs-cTnI levels.

STATISTICAL ANALYSIS

Data was analyzed using Statistical Package for the Social Sciences (SPSS) version 25. Mean & standard deviation were calculated for quantitative variables such as age, hs-cTnI levels, and SYNTAX score. Qualitative variables like gender, type of disease, artery involved, etc. were represented using frequency and percentage. The Chi-square test was applied to determine the relation between the variables such as hs-cardiac troponin I levels and SYNTAX score. Association of hs-cTnI levels with type of coronary artery disease was also determined. A p-value of ≤0.05 was taken as significant.

RESULTS

The mean age of patients was 61.82±8.94 years with a range of 43-80 years. Most of the patients [41(41%)] were between 51-60 years of age and 29(29%) patients were 61-70 years old. Eighty eight (88%) patients were females and only 12(12%) were males. Out of 100 patients, 68(68%) had both diabetes mellitus (DM) & hypertension (HTN), 20(20%) had only HTN, 2(2%) had DM, and 1(1%) was smoker. Thirty five (35%) patients had a positive family history of CAD.

The majority of the patients [36(36%)] had double vessel coronary artery disease (DVCAD), 32(32%) had triple vessel coronary artery disease (TVCAD) and 32(32%) had single vessel coronary artery disease (SVCAD). The left anterior descending artery (LAD) was involved in 50% followed by the left circumflex artery (LCX) in 21% and the right coronary artery (RCA) in 29% of the cases. The site of the lesion was proximal in 54%, middle in 15%, and distal in 31% of the patients. These results are tabulated in Table 1.

The mean SYNTAX score was 21.30±8.56 with the range of 5 to 45. The majority of the patients (50%) had SYNTAX scores of 0-22 and 35% had score of 23-32. Only 15% of the patients had a SYNTAX score >33.

The mean hs-cTnI level was 24.68±8.69 ng/L with a lowest level of 16.10 ng/L and maximum level of 40 ng/L. The mean hs-cTnI level in females was 20.70±5.65 ng/L with a minimum level of 16.10 ng/L and maximum level of 30.60 ng/L. The mean hs-cTnI in males was 37.28±2.11 ng/L ranging from 34.5 to 40 ng/L. A significant association existed between the disease severity indicated by the SYNTAX score and hs-cardiac troponin I levels. Patients with higher SYNTAX score had higher hs-cTnI levels (Table 2).

Similarly, a significant association was found between the type of disease (SVCSD, DVCAD, and TVCAD) and hs-cTnI levels. Patients with TVCAD had higher hs-cTnI levels as compared to patients with SVCAD and DVCAD (Table 3).

Table 1: Demographic Profile of the Study Participants

Variables		Descriptive Statistics
Age (Years)	**Mean±SD**	61.82±8.94
	41-50	10(10%)
	51-60	41(41%)
	61-70	29(29%)
	71-80	20(20%)
Gender	**Male**	12(12%)
	Female	88(88%)
Risk Factors	**No Risk Factor**	7(7%)
	HTN	20(20%)
	DM	2(2%)
	HTN & DM	68(68%)
	HTN & Smoking	1(1%)
	HTN & Obesity	1(1%)
	HTM, DM & Smoking	1(1%)
Family History of CAD	**Positive**	35(35%)
	Negative	65(65%)
Type of Disease	**SVCAD**	32(32%)
	DVCAD	36(36%)
	TVCAD	32(32%)
Artery Involved	**LAD**	50(50%)
	LCX	21(21%)
	RCA	29(29%)
Site of Lesion	**Proximal**	54(54%)
	Mid	15(15%)
	Distal	31(31%)

Table 2: Association of hs-cTnI Levels with the SYNTAX Score

hs-cTnI level (ng/L)		SYNTAX Score			Total	Chi-Square Statistic	p-value
		0-22	23-32	>33			
Females	**<20**	30(34.1%)	3(3.4%)	2(2.2%)	35(39.8%)	31.629	0.001*
	≥20	13(14.8%)	27(30.7%)	13(14.8%)	53(60.2%)		
	Total	43(48.9%)	30(34.1%)	15(17%)	88(100%)		
Males	**<38**	5(41.7%)	0(0%)	0(0%)	5(41.7%)	6.122	0.013*
	≥38	2(16.6%)	5(41.7%)	0(0%)	7(58.3%)		
	Total	7(58.3%)	5(41.7%)	0(0%)	12(100%)		

**Significant p-value*

Table 3: Association of hs-cTnI Levels with the Type of Disease

hs-cTnI level (ng/L)		Type of Disease			Total	Chi-square Statistic	p-value
		SVCAD	DVCAD	TVCAD			
Females	**<20**	22(25%)	10(11.4%)	3(3.4%)	35(39.8%)	27.208	0.001*
	≥20	7(8%)	19(21.6%)	27(30.6%)	53(60.2%)		
	Total	29(33%)	29(33%)	30(34%)	88(100%)		
Males	**<38**	3(25%)	2(16.6%)	0(0%)	5(41.7%)	6.122	0.047*
	≥38	0(0%)	5(41.7%)	2(16.6%)	7(58.3%)		
	Total	3(25%)	7(58.3%)	2(16.6%)	12(100%)		

**Significant p-value*

DISCUSSION

Higher levels of high-sensitivity cardiac troponin I are linked with CAD and increased chances of developing adverse outcomes such as recurrent episodes and cardiovascular mortality.[12] In this study, a association between hs-TnT and the severity of coronary artery disease was observed.

In our study, 88% were females and 12% were males, the mean age being 61.82±8.94 years. On the contrary, in another study, the majority of the patients (73.4%) were males and only 26.5% were

females with a mean age of 59.35±11.08 years.[10] Ali et al. included 204 patients in their study. The mean age of the patients was 67.4±14.5 years and 109(53.4%) patients were males.[13] The average age was 60 years and 85% were males according to AbdelHamid et al.[14] In our study, 68% of the patients had both DM & HTN, 20(20%) had only HTN, 2(2%) had DM and 1(1%) were smokers. Thirty five (35%) patients had a positive family history of CAD. According to Hasan et al., 50% of the cases were diabetic, 69.5% were hypertensive, and 63.9% had deranged lipid profiles. Around 28% of the patients were smokers and 22.2% had a positive history of CAD.[10] According to another study, 70% of the patients were smokers and had deranged lipid profiles. Around 38% of the patients had HTN and DM. A family history of CAD was positive in 24% of the cases.[14]

In our study, the majority of the patients had DVCAD (36%), 32% had SVCAD, and 32% had TVCAD. In another study, TVCAD, DVCAD, and single vessel disease were seen in 26%, 20%, and 20% of the patients, respectively. Normal angiograms were seen in 11% of patients, whereas 23% had non-obstructive CAD.[15] In our study, LAD was involved in 50% of the cases, LCX in 21%, and RCA in 29% of the cases. In another study, the artery predominantly involved was LAD (46.5%) followed by RCA (27.9%) and LCX (25.6%).[14] In a study by Samman Tahhan et al., LAD was involved in most of the patients.[15]

Our results showed that the mean SYNTAX score was 21.30±8.56. Another study reported a mean SYNTAX score of 17.3.[16] In another study, the average SYNTAX score was 16.5± 7.5.[15] Our study found a significant association between hs-troponin I levels and severity of disease, as indicated by SYNTAX score. Two other studies also revealed a positive link between hs-troponin I and SYNTAX score.[17,18] Another study reported a weak significant association between hs-troponin I and SYNTAX score but this study enrolled all patients with acute coronary syndrome.[19] Hasan et al. also reported a significant correlation between troponin I & SYNTAX score. But this relation was seen with troponin I, not hs-troponin I.[10] A significant relation was seen between hs-TnI levels and severity of CAD in a study but the severity of disease was assessed by the Gensini score, instead of SYNTAX score used in our study.[15] In contrast, no significant association was seen between SYNTAX score and hs-troponin I in a study by AbdelHamid et al. They enrolled both STEMI and NSTEMI patients rather than only patients with NSTEMI.[14] The results of a systematic review and meta-analysis revealed a positive relation between the severity of coronary artery disease and levels of hs-troponin I.[20]

Our results showed that the hs-cardiac troponin I level also had a significant relation with the type of disease i.e. SVCAD, DVCAD & TVCAD. Patients with triple vessel disease had significantly high hs-cTnI levels as compared to double vessel CAD & single vessel CAD. In another study, patients with triple vessel disease had significantly higher hs-troponin I levels.[15] Similar Hasan et al. also revealed a positive relation of TVCAD with hs-troponin I levels.[10]

CONCLUSION

High-sensitivity cardiac troponin I is a reliable marker of the severity of CAD. A significant association exists between the severity of disease as indicated by SYNTAX score and hs-cardiac troponin I levels in patients with NSTEMI. Patients with triple vessel disease are more likely to have higher hs-cardiac troponin I levels.

LIMITATIONS & RECOMMENDATIONS

This single-centered study was conducted at a tertiary care hospital. A multi-centered study should be conducted in the future. Follow-up of the patients was not done and the study did not evaluate the prevalence of adverse cardiac events in patients with elevated levels of hs-cardiac troponin I. Further study needs to be done to find out if patients with higher levels of hs-cardiac troponin I experience adverse cardiac events at follow-up. High-sensitivity cardiac troponin I should be employed instead of cardiac troponin I as a diagnostic aid in NSTEMI and to assess the severity of the disease.

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Authors' Contributions:

W.M: Drafting the work
M.R: Conception or design of the work
A.H: Drafting the work
W.A.L: Analysis or interpretation of data for the work
W.H: Analysis or interpretation of data for the work
A.M: Final approval and article revisions

REFERENCES

1. Ralapanawa U, Kumarasiri PVR, Jayawickreme KP, Kumarihamy P, Wijeratne Y, Ekanayake M, et al. Epidemiology and risk factors of patients with types of acute coronary syndrome presenting to a tertiary care hospital in Sri Lanka. BMC Cardiovasc Disord. 2019; 19(1):229. doi:10.1186/s12872-019-1217-x.

2. Agrawal A, Lamichhane P, Eghbali M, Xavier R, Cook DE, Elsherbiny RM, et al. Risk factors, lab parameters, angiographic characteristics and outcomes of coronary artery disease in young South Asian patients: a systematic review. J Int Med Res. 2023; 51(8):3000605231187806. doi:10.1177/03000605231187806.

3. Wu P, Yu S, Wang J, Zou S, Yao DS, Xiaochen Y. Global burden, trends, and inequalities of ischemic heart disease among young adults from 1990 to 2019: a population-based study. Front Cardiovasc Med. 2023; 10:1274663. doi:10.3389/fcvm.2023.1274663.

4. Thygesen K, Alpert JS, Jaffe AS, Chaitman BR, Bax JJ, Morrow DA, et al. Fourth universal definition of myocardial infarction (2018). Circulation. 2018; 138(20):e618-51. doi:10.1161/CIR.0000000000000617.

5. Tsai MK, Lai CH, Hung CL, Wu KY. Troponin I cutoff for non-ST-segment elevation myocardial infarction in sepsis. Mediators Inflamm. 2022; 2022:5331474. doi:10.1155/2022/5331474.

6. Eggers KM, Hammarsten O, Lindahl B. Differences between high-sensitivity cardiac troponin T and I in stable populations: underlying causes and clinical implications. Clin Chem Lab Med. 2022; 61(3):380-7. doi:10.1515/cclm-2022-0778.

7. Salimi A, Zolghadrasli A, Jahangiri S, Hatamnejad MR, Bazrafshan M, Izadpanah P, et al. The potential of HEART score to detect the severity of coronary artery disease according to SYNTAX score. Sci Rep. 2023; 13(1):7228. doi:10.1038/s41598-023-34213-9.

8. Ozturk S, Gurbuz AS, Kırma C. Relationship between SYNTAX score and myocardial viability in ischemic cardiomyopathy. Turk Kardiyol Dern Ars. 2019; 47(5):350-6. doi:10.5543/tkda.2019.88054.

9. Khan R, Akhter J, Munir U, Almas T, Ullah W. Frequency of non-ST segment elevation myocardial infarction (NSTEMI) in acute coronary syndrome with normal electrocardiogram (ECG): insights from a cardiology hospital in Pakistan. Cureus. 2020; 12(6):e8758. doi:10.7759/cureus.8758.

10. Hasan KM, Rahmat Ullah A, Ziaul SMH, Tanveer A, Souman C, Reazur R, et al. Correlation of raised cardiac Troponin I (50 folds upper limit of normal) and elevated SYNTAX score for extent and severity of coronary artery disease in first attack of NSTEMI in Bangladeshi population. German International Journal of Modern Science. 2021; 17:15-23. doi:10.24412/2701-8369-2021-17-15-23.

11. Lee KK, Ferry AV, Anand A, Strachan FE, Chapman AR, Kimenai DM, et al. Sex-specific thresholds of high-sensitivity troponin in patients with suspected acute coronary syndrome. J Am Coll Cardiol. 2019; 74(16):2032-43. doi:10.1016/j.jacc.2019.07.082.

12. Mohebi R, Jackson L, McCarthy CP, Murtagh G, Murphy SP, Abboud A, et al. Relation of high-sensitivity cardiac troponin I and obstructive coronary artery disease in patients without acute myocardial infarction. Am J Cardiol. 2022; 173:16-24. doi:10.1016/j.amjcard.2022.03.001.

13. Ali F, Arshad K, Szpunar S, Daher E. Elevated troponins and diagnosis of non-ST-elevation myocardial infarction in the Emergency Department. Cureus. 2024; 16(5): e59910. doi:10.7759/cureus.59910.

14. AbdelHamid I, Amin YM, Tamara AF. Correlation between high-sensitive troponin level, neutrophil lymphocyte ratio and SYNTAX score in acute myocardial infarction patients undergoing coronary angiography. EJHM. 2023; 90(1): 1809-13. doi:10.21608/EJHM.2023.284332.

15. Samman Tahhan A, Sandesara P, Hayek SS, Hammadah M, Alkhoder A, Kelli HM, et al. High-sensitivity troponin I levels and coronary artery disease severity, progression, and long-term outcomes. J Am Heart Assoc. 2018; 7(5):e007914. doi:10.1161/JAHA.117.007914.

16. Xu M, Chen H, Li HW. The association between SYNTAX score and long-term outcomes in patients with unstable angina pectoris: a single-centre retrospective study. BMC Cardiovasc Disord. 2022; 22(1):155. doi:10.1186/s12872-022-02604-x.

17. Cardoso MR, da Silva Junior DG, Ribeiro EA, da Rocha Neto AM. Correlation between the complexity of coronary lesions and high-sensitivity troponin levels in patients with acute coronary syndrome. IJCS. 2018; 31(3)218-25. doi:10.5935/2359-4802.20180014.

18. Bay B, Goßling A, Blaum CM, Kroeger F, Koppe L, Lorenz T, et al. Association of high-sensitivity troponin T and I blood concentrations with all-cause mortality and cardiovascular outcome in stable patients-results from the INTERCATH Cohort. J Am Heart Assoc. 2022; 11(17):e024516. doi:10.1161/JAHA.121.024516.

19. Ho AB, Tran QB. The role of N-terminal-pro-B-type natriuretic peptide (NT-proBNP) and high-sensitivity troponin T (hs-troponin T) in the evaluation of the SYNTAX score in patients with acute coronary syndrome. Cureus. 2024; 16(3):e55653. doi:10.7759/cureus.55653.

20. Fatemi A, Zahedi M, Yazdooei Y, Daei M, Ansari MM, Sohrabi A, et al. Association between high-sensitive cardiac troponin level and coronary artery disease: a systematic review and meta-analysis. JRSM Cardiovasc Dis. 2023; 12:20480040231220094. doi:10.1177/20480040231220094.

Original Article

Comparative Analysis of Lay Open versus Primary Closure Techniques in the Management of Sacrococcygeal Pilonidal Sinus

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ABSTRACT

Objective: To compare the outcome of surgery in patients with pilonidal sinus managed with lay open approach versus primary closure technique.

Methodology: This quasi-experiment was conducted at the Department of Surgery, Bahawal Victoria Hospital, Bahawalpur from June 2021 to September 2023 after ethical approval. A total of 102 patients of both genders with an age range of 20-60 years presenting with pilonidal sinus were included by non-probability convenient sampling technique. Patients with a history of previous spine surgery, chemotherapy, and immunocompromised medical conditions like lymphoma, leukemia, and acquired immunodeficiency syndrome (AIDS) were excluded from the study. Two groups of patients were formed (groups A and B). Group A included patients treated with lay open approach and in group B, the primary closure technique was used. Total hospital stay and time to return to normal activities were documented. Patients were seen on the 3rd, 7th, 10th day, one month, and six months after the surgery to observe any evidence of wound infection, healing time (days), and recurrence. Data was analyzed using Statistical Package for the Social Sciences (SPSS) version 26.

Results: Group A had a mean hospital stay of 4.47±1.53 days, whereas in group B, it was 3.00±1.15 days. A statistically significant difference was found in the comparison of mean hospital stay in both groups (p-value <0.0001). The mean time to return to normal activities was 11.98±2.53 days in group A and 8.27±1.97 days in group B (p-value <0.0001). The surgical wound in group A patients took an average of 33.25±3.96 days to heal, whereas in group B, the average wound healing time was 14.94±2.24 days. This difference was statistically significant (p-value <0.0001). Six (11.8%) patients in group A and 3(5.9%) patients in group B had postoperative wound infections (p-value=0.295). Five (9.8%) patients in group A and 3(5.9%) patients in group B had recurrences of the sacrococcygeal pilonidal sinus illness (p-value=0.461).

Conclusion: Excision with primary closure of the pilonidal sinus is a superior technique as compared to the lay open approach in terms of reduced hospital stay, better healing time, and earlier return to normal activities.

Keywords: *Pilonidal sinus. Surgical procedures. Recurrence. Infections.*

INTRODUCTION

Pilonidal sinus, a frequently encountered surgical ailment, originates from the follicles of hair nestled in the sacrococcygeal area.[1] While the precise causes of pilonidal disease remain the subject of debate, there is a strong consensus regarding the involvement of loose hair implantation into the skin of the sacrococcygeal area.[2] The historical roots of pilonidal disease date back to 1833 when Mayo first described it, suggesting its congenital origin linked to the remnants of an epithelial-lined tract.[3] However, the literature showed that the main causes of pilonidal sinus are local trauma, poor hygiene, thick body hair, or the existence of a deep birth cleft. Males, young age, overweight, hirsutism, and positive family history are the risk factors to acquire this disorder.[4] Patients with pilonidal sinus have a range of symptoms from asymptomatic pits to discharging sinuses, abscesses, and pilonidal cysts.[5] Surgeons may have different approaches to treat the illness, but the basic treatment guidelines are always the same: clearing the infected sinus tract, fully mending the skin that covers it, and reducing the likelihood of recurrence. Postoperative complications are mostly wound infections and substantial recurrence rates following surgery.[6]

The ultimate goal in managing pilonidal sinus disease is to achieve a durable cure, minimize recurrence, shorten hospital stays, and expedite a return to normal activities. Various surgical options including lay open the sinus tract, marsupialization, excision with primary repair, the Bascom procedure, Karydakis flap, Limberg flap, and laser surgery are available.[7] Each of these procedures possess merits and demerits, rendering none as a universally

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acknowledged gold standard. Lay open of the surgical incision might be followed by its healing. This method has the benefit of lessening wound tension, which speeds up the healing process and stops recurrence. Alternatively, primary closure can be used to seal the wound.[5]

Despite the array of techniques used to manage pilonidal sinus, a definitive approach remains elusive. This study delves into the comparative evaluation of two management methods for pilonidal sinus within our local context. By providing objective data from our region, this study will help us to use a better technique in treating pilonidal sinus associated with early recovery, lesser side effects & recurrence.

METHODOLOGY

This quasi-experiment was conducted at the Department of Surgery, Bahawal Victoria Hospital, Bahawalpur from June 2021 to September 2023. A sample size of 102 was estimated by using a 95% confidence interval, 80% power with an expected infection rate of 7.1% and 25% in primary closure and open group, respectively.[8] Non-probability convenient sampling technique was used. Patients of both male & female gender and 20-60 years of age presenting with pilonidal sinus and American Society of Anesthesiologists (ASA) status I & II were included. Patients with recurrent pilonidal sinus, history of previous spine surgery, chemotherapy, and immunocompromised medical conditions like lymphoma, leukemia, and AIDS were excluded from the study.

The study was approved by the ethical review committee of the institution (Letter No: 1164/DME/QAMC Bahawalpur, 10-05-2021). Patients were divided into two groups: Group A & group B. Every patient provided informed written consent. Patients in group A were treated with lay open procedure, whereas patients in group B received primary closure management. Both methods were technically carried out in accordance with the applicable “standard procedure”. Methylene blue was injected into the sinus before excision to ensure thorough removal of the affected tissue, while preserving the skin. The procedure was considered complete for patients in group A, and wounds were packed, dressed, and allowed to heal through secondary intention. In contrast, patients in group B had their skin edges slightly undermined and had the full thickness of their wound edges closed in the middle by proline no. 1 tie over sutures, which went through the presacral fascia in the center of the wound cavity. Absorbable 2/0 stitches were used to seal the core incision after meticulous hemostasis was maintained throughout the process. Stitches were taken out at the 10^{th} postoperative day.

Pilonidal sinus is defined as a subcutaneous skin infection in the gluteal sulcus of the sacrococcyx characterized by pain [visual analog scale (VAS) >3], redness, and discharge of fluid, diagnosed clinically by a consultant surgeon having at least three years of post-fellowship experience. Patient was labelled as positive for wound infection who had any of the following; total leukocyte counts more than 11000/cm^3, history of fever documented with temperature more than 99ºF, presence of inflammatory signs around wound like erythema, warmth, and evidence of pus oozing from the wound.[9] Length of hospital stay was counted from the day of the procedure to the discharge of the patient (when the patient was hemodynamically & clinically stable and could walk at least 50 meters). Total hospital stay (days) was also documented. Patients were seen on the 3^{rd}, 7^{th}, 10^{th} day, one month, and six months of surgery to see any evidence of wound infection, healing status, return to normal activity, and recurrence.

STATISTICAL ANALYSIS

Data was analyzed using Statistical Package for the Social Sciences (SPSS) version 26. Quantitative variables like age, duration of disease, hospital stay, time to return to normal activities, and healing time were presented as mean±standard deviation, while qualitative variables like gender, wound infection, and recurrence were presented as frequency and percentage. Comparison of hospital stay, return to normal activities, and healing time between both groups was done by Independent t-test, whereas comparison of wound infection and recurrence between the study groups was done by Chi-square test. A p-value of ≤0.05 was considered significant.

RESULTS

A total of 102 patients with a mean age of 38.93±7.72 years and an age range of 20-60 years were enrolled. The mean age of the patients in group A was 38.76±7.44 years, while it was 39.27±8.04 years in group B. Table 1 reveals that the majority of

the patients (58.82%) were in the 20-40 years age range. There were 93(91.18%) male and 9(8.82%) female patients with a male-to-female ratio of 10.3:1. Patients in the study had a mean duration of disease of 7.13±2.39 months. In group A, the mean duration was 6.96±2.33 months, whereas in group B, it was 7.35±2.53 months. In group A, the mean body mass index was 30.12±3.35 kg/m^2, whereas in group B, it was 30.24±3.25 kg/m^2. No significant difference was found between the study groups (p-value=0.8547)

Table 2 shows that the mean hospital stay for group A was 4.47±1.53 days, while the mean hospital stay for group B was 3.00±1.15 days. A statistically significant difference was found in the mean hospital stay between the two groups (p-value <0.0001). In group A, the mean time to return to normal activities was 11.98±2.53 days, whereas in group B, it was 8.27±1.97 days (p-value <0.0001). The mean healing time of surgical wound was 33.25±3.96 days in group A as compared to 14.94±2.24 days in group B. This difference was statistically significant (p-value <0.0001).

Six (11.8%) patients in group A and 3(5.9%) patients in group B had postoperative wound infections (p-value=0.295). The sacrococcygeal pilonidal sinus disease recurrence occurred in 5(9.8%) patients in group A and 3(5.9%) patients in group B (Table 2).

DISCUSSION

The present study delved into a comprehensive comparison between two prominent surgical techniques employed in managing pilonidal sinus. The demographic data of the patients enrolled in this study showed that the prevalence of pilonidal sinus among young adults was predominantly in males. Similar results were seen in another study conducted by Doll et al. in 2019.[10]

Results of our study showed that the number of days of hospital stay and number of days for return to normal activities were better in primary closure. The difference was statistically significant (p-value <0.05). Similarly wound healing time was also significantly better in group B (p-value <0.05). Recurrence and wound healing rates were comparable between the primary closure and lay open technique groups.

Table 1: Age Distribution for Study Participants

Age (Years)		Group A (n=51)	Group B (n=51)
Groups	**20-40**	31(60.78%)	29(56.86%)
	41-60	20(39.22%)	22(43.14%)
Mean±SD		38.76±7.44	39.27±8.04

Table 2: Study Variables of both Groups

Study Variables		Group A	Group B	p-value
Hospital Stay (Days)	**Mean±SD**	4.47±1.53	3.00±1.15	<0.0001*
Return to Normal Activity (Days)	**Mean±SD**	11.98±2.53	8.27±1.97	<0.0001*
Healing Time (Days)	**Mean±SD**	33.25±3.96	14.94±2.24	<0.0001*
Wound Infection	**Frequency & Percentage**	6(11.8%)	3(5.9%)	0.295
Recurrence	**Frequency & Percentage**	5(9.8%)	3(5.9%)	0.461

**Significant p-value*

Gips et al. study included 320 patients and compared open & primary closure techniques. They reported that the mean duration of return to normal activity was significantly decreased in the primary closure group (p=0.002). The operative time was statistically high in primary closure (p=0.001). However, the main closure approach had a greater recurrence rate as compared to the open technique (p-value=0.009). The difference might be due to patient related factors.[11]

Our study meticulously examined wound healing time, a pivotal parameter in evaluating the efficacy of surgical interventions. Healing time was prolonged in group A (33.25±3.96 days) as

compared to group B (14.94±2.24 days). This accelerated healing not only diminishes the physical discomfort experienced by the patients but also minimizes the risk of secondary infections, thereby enhancing overall postoperative recovery. According to another study, the median wound healing time was 49 days for the open method group and 14 days for the closed method group. There was no difference in the recurrence rate between the two groups.[12] A study by Chopade et al. reported that the mean healing time in the open method was 57±11 days, while it was 20±2 days in the closed method group. Duration of work loss was also reported to be significantly higher in the open group. They reported no recurrence in both methods.[13] Another study included 78 patients with primary closure and excision of pilonidal disease. According to that study, the average length of hospital stay was 2.5 days, and most of the patients were discharged within three weeks to resume their regular lives or jobs. The wound infection rate was 6.41%, while the recurrence rate was 3.85%.[14]

In a study by Bubenova et al., a total of 382 patients underwent surgery for pilonidal disease at the Medical University of Vienna. The recurrence rate in the primary excision with the primary midline closure group was 24.7%, while the open method group had a recurrence of 18.1%. The primary midline closure group had a high wound infection rate of 46.3%, while in the open method group, the wound infection rate was 23.9%.[15]

Anandaravi et al. reported a better would healing for excision using the main closure (14.2 days) as compared to open healing (51.6 days) methods. The results were in similarity with our study. Length of hospital stay found in this study was almost similar to our results. In the open group, it took an average of 34 days to return to work, compared to 8 days in the primary closure groups. Primary closure is a better surgical method as compared to the lay open technique for the management of pilonidal sinus in the sacrococcygeal area. The recurrence rate, a pivotal factor in assessing the long-term success of any surgical procedure was found to be comparable between the two groups. This suggests that while the primary closure method offers expeditious healing and reduced hospital stay, it does not compromise the recurrence rates, signifying its stability as a treatment option.[16]

CONCLUSION

Excision with primary closure of the pilonidal sinus is a superior technique as compared to the lay open approach in terms of reduced hospital stay, better healing time, and earlier return to normal activities.

LIMITATIONS & RECOMMENDATIONS

The single-centered research design may restrict the generalizability of our results and the limited sample size may have an impact on statistical power, particularly for less common outcomes like wound infection and recurrence. The short follow-up duration might not capture long-term outcomes adequately. Future research should prioritize multi-centered collaborations to enhance diversity and increase sample sizes. Longer follow-up periods would provide more comprehensive insights. Implementing blinding procedures can mitigate bias and exploring novel techniques may offer alternative approaches to improving outcomes and reducing recurrence rates.

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Authors' Contributions:

T.I: Substantial contributions to the conception of the work

S.U.M: Acquisition, analysis, and interpretation of data for the work

M.T: Acquisition, analysis, and interpretation of data for the work

M.S: Revising the work critically for important intellectual content

Z.M: Revising the work critically for important intellectual content

F.M.A: Final approval of the version to be published

REFERENCES

1. Berthier C, Berard E, Meresse T, Grolleau JL, Herlin C, Chaput B. A comparison of flap reconstruction vs the laying open technique or excision and direct suture for pilonidal sinus disease: a meta-analysis of randomised studies. Int Wound J. 2019; 16(5):1119-35. doi:10.1111/iwj.13163.

2. Obokhare I, Amajoyi RC. Pilonidal disease: to flap or not to flap. Adv Surg. 2023; 57(1):155-69. doi:10.1016/j.yasu.2023.04.011.

3. Wu P, Zhang Y, Zhang Y, Wang S, Fan Z. Progress in the surgical treatment of sacrococcygeal pilonidal sinus: a review. Int J Surg. 2023; 109(8):2388-403. doi:10.1097/JS9.0000000000000447.

4. Odlo M, Horn J, Xanthoulis A. Surgery for pilonidal sinus disease in Norway: training, attitudes and preferences-a survey among Norwegian surgeons. BMC Surg. 2022; 22(1):442. doi:10.1186/s12893-022-01889-1.

5. Bi S, Sun K, Chen S, Gu J. Surgical procedures in the pilonidal sinus disease: a systematic review and network meta-analysis. Sci Rep. 2020; 10(1):13720. doi:10.1038/s41598-020-70641-7.

6. Garg P, Yagnik VD. Laying open and curettage under local anesthesia to treat pilonidal sinus: long-term follow-up in 111 consecutively operated patients. Clin Pract. 2021; 11(2):193-9. doi:10.3390/clinpract11020028.

7. Popeskou SG, Pravini B, Panteleimonitis S, Vajana AFDT, Vanoni A, Schmalzbauer M, et al. Conservative sinusectomy vs. excision and primary off-midline closure for pilonidal disease: a randomized controlled trial. Int J Colorectal Dis. 2020; 35(7):1193-9. doi:10.1007/s00384-020-03551-9.

8. Eldsoky ES, Atwa NS, Naroz MI, Hifny A. Comparative study between excision with primary closure versus flap reconstruction in management of sacrococcygeal pilonidal sinus. SJMS. 2021; 2021(1):13-22. doi:10.55675/sjms.v2021i1.45.

9. Li Z, Jin L, Gong T, Qin K, Cui C, Wang Z, et al. An effective and considerable treatment of pilonidal sinus disease by laser ablation. Lasers Med Sci. 2023; 38(1):82. doi:10.1007/s10103-023-03741-1.

10. Doll D, Orlik A, Maier K, Kauf P, Schmid M, Diekmann M, et al. Impact of geography and surgical approach on recurrence in global pilonidal sinus disease. Sci Rep. 2019; 9(1):15111. doi:10.1038/s41598-019-51159-z.

11. Gips M, Bendahan J, Ayalon S, Efrati Y, Simha M, Estlein D. Minimal pilonidal surgery vs. common wide excision operations: better well-being and comparable recurrence rates. Isr Med Assoc J. 2022; 24(2):89-95. Available from: https://api.semanticscholar.org/CorpusID:247010460.

12. Hemmingsson O, Binnermark F, Odensten C, Rutegard M, Franklin KA, Haapamaki MM. Excision and suture in the midline versus Karydakis flap surgery for pilonidal sinus: randomized clinical trial. BJS Open. 2022; 6(2):zrac007. doi:10.1093/bjsopen/zrac007.

13. Chopade SP, Adhikari GR. Comparative study of Limberg flap reconstruction with wide-open excision and healing by secondary intention in the management of pilonidal sinus: our experience at a tertiary care center in India. Cureus. 2022; 14(6):e26396. doi:10.7759/cureus.26396.

14. Alkatta MA, Mejally A. Excision and tension-free primary closure of pilonidal disease. Turk J Surg. 2019; 35(4):278-84. doi:10.5578/turkjsurg.4368.

15. Bubenova M, Mittlboeck M, Kulinna-Cosentini C, Teleky B, Cosentini E. Pilonidal sinus disease: a 25-year experience and long-term results of different surgical techniques. Eur Surg. 2022; 54(5):240-8. doi:10.1007/s10353-022-00767-7.

16. Anandaravi BN, Viswanathan A. Comparative study between excision with lay open and excision with primary closure in treatment of pilonidal sinus. Int Surg J. 2019; 6(4):1242-6. doi:10.18203/2349-2902.isj20191256.

Original Article

Antimicrobial Susceptibility Pattern of Extended-Spectrum Beta-Lactamase Producing *Escherichia coli* in Urinary Tract Infection

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ABSTRACT

Objective: To detect the frequency of extended-spectrum beta-lactamase (ESBL) producing *Escherichia coli* in urinary tract infection and also determine their antibiotic susceptibility to various antimicrobials.

Methodology: This cross-sectional study was conducted at the Microbiology Department of Federal Government Polyclinic Hospital, Islamabad from January to June 2023 after ethical approval. By non-probability convenient sampling, 1410 positive urine cultures with the growth of *Escherichia coli* (*E. coli)* were included. Antibiotic sensitivity testing was performed. Extended-spectrum beta-lactamase testing was conducted using ceftazidime (30 µg) and cefotaxime (30 µg) alone and in combination with clavulanate as per the Clinical and Laboratory Standards Institute (CLSI) guidelines 2022. The data was compiled using the Statistical Package for the Social Sciences (SPSS) version 25.

Results: Out of 1410 *E. coli*, 830(58.9%) strains were ESBL producing, while 580(41.1%) were ESBL negative. Extended-spectrum beta-lactamase production had no association with age, gender, marital status, and residence. The antibiotic sensitivity of ESBL positive isolates revealed 100% sensitivity to meropenem and 97.6% sensitivity to imipenem. The sensitivity of isolates to nitrofurantoin was 93%, amikacin was 80.2%, and gentamicin was 66.3%. Only a small percentage of *E. coli* were sensitive to ciprofloxacin (37.2%) and trimethoprim-sulfamethoxazole (23.3%).

Conclusion: The frequency of ESBL producing *E. coli* was very high (58.9%) in our study. Meropenem, imipenem, nitrofurantoin, and amikacin can be used to treat these organisms. Besides being resistant to beta-lactam drugs, *E. coli* also showed poor sensitivity results to trimethoprim-sulfamethoxazole (23.3%) and ciprofloxacin (37.2%).

Keywords: *Meropenem. Escherichia coli. Urinary tract infections.*

INTRODUCTION

Urinary tract infections caused by multidrug-resistant organisms are the most common infections with high prevalence of *E. coli* ranging from 70-90% worldwide.[1] Immediate therapy with an appropriate antimicrobial can help to prevent the complications of the infection such as progressive renal damage and renal failure.[2] The antibiotics used frequently against *E. coli* are β-lactams, tetracyclines, fluoroquinolones, co-trimoxazole, and aminoglycosides. However, the increasing trend of antimicrobial resistance among *E. coli* has led to limited antibiotics available for treatment.[3]

Antibiotic resistance is a challenging public problem leading to 700,000 deaths per year.[4] Extended-spectrum beta-lactamase positive gram-negative rods are the main class among antibiotic-resistant strains.[5] This enzyme confers resistance to beta-lactam antibiotics and monobactams by breaking down the beta-lactam ring of these antibiotics but not to carbapenems.[6] The enzyme is inhibited by beta-lactamase inhibitor such as clavulanic acid or tazobactam.[7] The ESBL genes are present on plasmids which are readily transmissible among bacteria and also attribute resistance to other antibiotics as well.[8] The frequency of ESBL positive bacteria is rising across the world. *Escherichia coli* is the most common bacterium harbouring the ESBL gene and causes multidrug resistant infections.[7] Around 60% of the ESBL producing *E. coli* arise from the genitourinary source.[9] Extended-spectrum beta-lactamase producing *E. coli* poses a significant challenge like treatment failure, high risk of poor outcomes, and greater morbidity & mortality.[3] Infections caused by such strains also lead to a significant financial burden by increasing the duration of hospital stay and expenditure due to the use of multiple antibiotics.[10]

The high frequency of ESBL positive infections has resulted from the overuse of antibiotics, necessitating judicious use of appropriate antibiotics based on antibiotic susceptibility results.[11] This study was done to detect the frequency of ESBL producing *E. coli* in urinary tract infections and also determine their antibiotic susceptibility to other antimicrobials. The surveillance of antibiotic-resistant organisms is very important in local settings as it guides clinicians regarding the empiric treatment regimen to be used for infections caused by these organisms.

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METHODOLOGY

This cross-sectional study was conducted at the Microbiology Department of Federal Government Polyclinic Hospital, Islamabad from January to June 2023. Permission was taken from the ethical committee of the hospital (Letter No: F004/06-2022, 10-06-2022). A total of 4000 urine samples were received in the laboratory and processed. Out of these, 2400(60%) samples revealed positive growth, whereas 1600(40%) samples had no growth. By non-probability convenient sampling, 1410(58.75%) positive urine cultures with the growth of *E. coli* were included.

Patients were guided to collect urine samples in sterilized plastic containers and their samples were sent to the microbiology laboratory for culture and sensitivity. Patients with gross or microscopic hematuria, pregnancy, history of renal stones, urinary tract instrumentation within 6 months, and those who took antibiotics in the last 2 weeks were excluded. Urine routine examination of samples was also done and findings were noted. In patients with urinary tract infection, leukocyte esterase was positive and microscopy revealed white blood cells (WBCs). The normal range of WBCs per high power field (40X) in a urine sample is 0-3 in males and 0-5 in females.[12] The urine samples were inoculated on cystine lactose electrolyte deficient (CLED) agar and incubated at 35-37°C for 24-48 hours.

The samples that revealed growth of lactose fermenting gram-negative rods were further proceeded. The biochemical tests applied to identify *E. coli* were triple sugar iron, citrate utilization, urease, indole, and motility tests. Antibiotic sensitivity testing was performed using the modified Kirby-Bauer disc diffusion method.[13] Bacterial suspensions of isolated *E. coli* equivalent to 0.5 Mcfarland turbidity standard were prepared and inoculated on Muller-Hinton agar and antibiotic discs were applied. Extended-spectrum beta-lactamase testing was conducted using ceftazidime (30 µg) and cefotaxime (30 µg) alone and in combination with clavulanate as per the CLSI guidelines 2022.[14]

STATISTICAL ANALYSIS

The data was compiled using the Statistical Package for the Social Sciences (SPSS) version 25. Mean±standard deviation was calculated for quantitative variables. Frequency & percentage were used for qualitative variables. Post-stratification Chi-square test was used to detect the association between ESBL production and other variables such as patient age, gender, residence, and marital status. A p-value of ≤0.05 was taken as significant.

RESULTS

All patients had a mean age of 41.81±17.48 years with minimum and maximum ages of 12 and 70 years. There were 599(42.5%) male and 811(57.5%) female cases with female dominance. Eight hundred and sixty nine (61.6%) belonged to urban areas, whereas 541(38.4%) were from rural areas. There were 889(63%) married and 521(37%) cases were unmarried. Out of 1410 *E. coli*, 830(58.9%) strains were ESBL producing, while 580(41.1%) were ESBL negative.

Data was stratified for age, gender, residence, and marital status. Statistically insignificant association was found when frequency of ESBL positive *E. coli* was compared with age groups (p=0.384), gender (p=0.399), residence (p=0.297), and marital status (p=0.14). Frequency of ESBL positive *E. coli* was statistically insignificant in both age groups [434(52.3%) versus 396(47.7%)], male [376(45.3%)] versus female [454(54.7%)], urban [482(58.1%)] versus rural [348(41.9%)], and married [482(58.1%)] versus unmarried [348(41.9%)]. These results are shown in Table 1.

The antibiotic sensitivity of ESBL positive isolates revealed 100% sensitivity to meropenem and 97.6% sensitivity to imipenem. The sensitivity of isolates to nitrofurantoin was 93%, amikacin was 80.2%, and gentamicin was 66.3%. Only a small percentage of *E. coli* were sensitive to ciprofloxacin (37.2%) and trimethoprim-sulfamethoxazole (23.3%) (Figure 1).

DISCUSSION

The increasing trend of ESBL positivity in *E. coli* poses a serious concern due to the failure of empiric therapy, limited treatment options, and complications.[15] The frequency of ESBL positive *E. coli* was very high (58.9%) in the present study. Similarly, ESBL positivity was 51%, and 56% in *E. coli* in other studies.[7,13] Shrestha et al. reported 50.9% of the ESBL positive *E. coli*.[16] Another study reported high prevalence of ESBL producing *E. coli* (62%) in Jordan.[17] The reported prevalence was 37.1% by Rajabnia et al. and 46.6% by Kumar et al., which are less than the frequency found in our study.[18,19] In another study, 23% of the urinary isolates were ESBL producing and out of these, 76.5% were *E. coli*.[20] In two other studies, 28% and 16% of *E. coli* were ESBL producing.[21,22] A study was conducted in Nepal in 2020 to determine the prevalence of ESBL production in *E. coli.* They found the highest ESBL production among *Klebsiella* (50%) and 27.9% by *E coli.* in the pediatric population.[3]

In our study, most of the ESBL positive *E. coli* were isolated from females and the most prevalent age group was 12-40 years. Abayneh et al. also reported ESBL positivity in 70.6% of the females and the average age was 35.07 years.[20]

Table 1: Association of Demographic Variables with ESBL Production

Study Variables		ESBL Production			Chi-Square Statistic	p-value
		Positive	Negative	Total		
Age Groups (Years)	12-40	434(52.3%)	261(45%)	695(49.3%)	0.759	0.384
	41-70	396(47.7%)	319(55%)	715(50.7%)		
	Total	830(100%)	580(100%)	1410(100%)		
Gender	Male	376(45.3%)	223(38.4%)	599(42.5%)	0.712	0.399
	Female	454(54.7%)	357(61.6%)	811(57.5%)		
	Total	830(100%)	580(100%)	1410(100%)		
Residence	Urban	482(58.1%)	387(66.7%)	869(61.6%)	1.08	0.297
	Rural	348(41.9%)	193(33.3%)	541(38.4%)		
	Total	830(100%)	580(100%)	1410(100%)		
Marital Status	Married	482(58.1%)	407(70%)	889(63%)	2.13	0.14
	Unmarried	348(41.9%)	173(30%)	521(37%)		
	Total	830(100%)	580(100%)	1410(100%)		

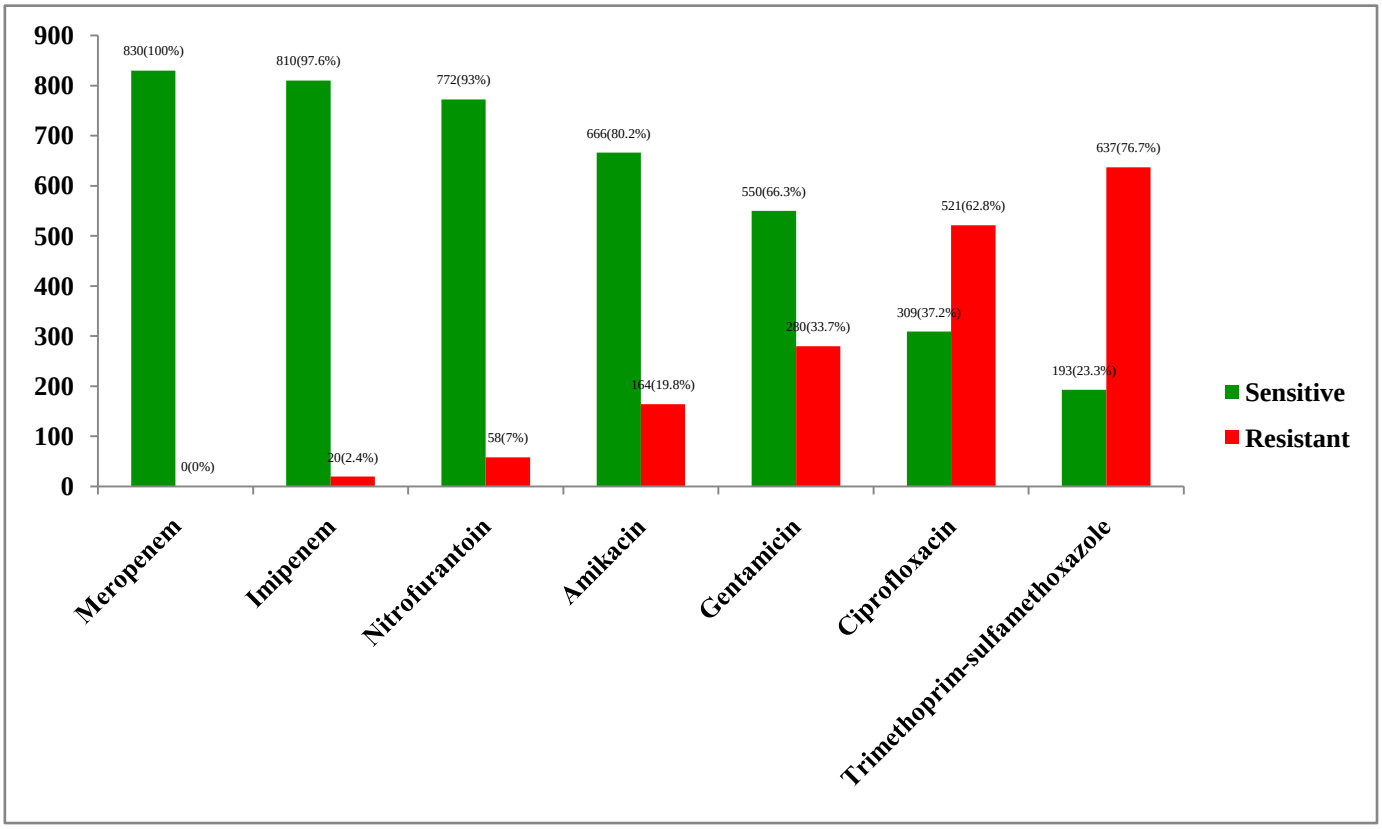

Figure 1: Antimicrobial Sensitivity of ESBL Producing *E. coli* [n=830]

Our results showed 100% sensitivity of ESBL producing *E. coli* to meropenem and 97.6% sensitivity to imipenem. The majority of the isolates were sensitive to nitrofurantoin (93%), amikacin (80.2%), and gentamicin (66.3%). Only a small percentage of *E. coli* were sensitive to ciprofloxacin (37.2%) and trimethoprim-sulfamethoxazole (23.3%). Hassuna et al. reported 100% sensitivity of ESBL strains to meropenem followed by ciprofloxacin (86.25%), ofloxacin (82.5%), and gentamicin (73.7%). Only 18.75% strains were sensitive to trimethoprim-sulfamethoxazole.[7] In a study conducted in UK, all the isolates of *E. coli* were sensitive to imipenem and only 14.2% isolates were nitrofurantoin resistant. The resistance to other antimicrobials was high: trimethoprim-sulfamethoxazole (62.8%), ciprofloxacin (60%), aminoglycosides (51.4%), tetracycline (57%).[23]

Meropenem also showed the best sensitivity results (93.5%) in another study followed by nitrofurantoin (81.48%) and gentamicin (55.56%), whereas ciprofloxacin and co-trimoxazole showed poor results with 21.1% and 15.7% sensitivity.[18] According to a study conducted in Bangladesh, 100% of the isolates were sensitive to imipenem, 95.7% to amikacin, and only 16.9% to ciprofloxacin.[24] Similarly another study showed 100% sensitivity of ESBL producing *E. coli* to imipenem and piperacillin/tazobactam, whereas 81% strains were resistant to ciprofloxacin, 61.5% to trimethoprim-sulfamethoxazole, 46.2% to tobramycin and 34.6% to gentamicin.[25] In a study by Besharati Zadeh et al., 32% of *E. coli* were resistant to gentamicin, 25% to amikacin, and 23% to ciprofloxacin.[21] Another study showed higher resistance of ESBL producing *E. coli* to quinolones (88.5%) and gentamicin (80.3%).[19]

Our study found no significant association of ESBL production with demographic variables such as age, gender, marital status, and residence. Similarly, a study by Abayneh et al. found no relation between ESBL positivity and demographic variables.[20] Kumar et al. reported that out of 131 *E. coli* isolates, 61(46.6%) were ESBL producers. They also revealed a significant relation between ESBL positivity with advanced age and high resistance in ESBL to non-beta-lactam antibiotic.[19] Kettani Halabi et al. conducted a study in Morocco to observe the antibiotic resistance of ESBL producing *E. coli*. isolates from patients with urinary tract infection. They included 670 urine samples, out of which 438(65%) were *E. coli* isolates. Extended-spectrum beta-lactamase positivity was seen in 259(59%) cultures showing *E. coli* growth. Contrary to our results, they also reported that female gender and age above 50 years were significantly associated with urinary tract infections caused by ESBL producing isolates with p-value=0.004 & p-value=0.001, respectively. All ESBL producing *E. coli* were resistant to amoxicillin, ticarcillin, and third generation cephalosporins. However, ESBL producing *E. coli* were 98% sensitive to ertapenem and 96% imipenem.[13]

CONCLUSION

The frequency of ESBL producing *E. coli* was very high (58.9%) in our study. Meropenem, imipenem, nitrofurantoin, and amikacin can be used to treat these organisms as the majority of these strains were sensitive to these antibiotics. Besides being resistant to beta-lactam drugs, *E. coli* also showed poor sensitivity results to trimethoprim-sulfamethoxazole (23.3%) and ciprofloxacin (37.2%).

LIMITATIONS & RECOMMENDATIONS

It was a single-centered study so its results cannot be generalized. Further studies involving multiple centers are recommended. Necessary steps should be taken at the national level to stop the rise in antimicrobial resistance. Over the counter availability of antibiotics and their inappropriate use should be limited, so as to combat the issue of antimicrobial resistance.

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Authors' Contributions:
T.H: Drafting the work
A.Z: Conception and design of the work
R.A: Drafting the work
H.A: Analysis and interpretation of data for the work
M.M: Analysis and interpretation of data for the work
M.N: Final approval and article revisions

REFERENCES

1. Larramendy S, Deglaire V, Dusollier P, Fournier JP, Caillon J, Beaudeau F, et al. Risk factors of extended-spectrum beta-lactamases-producing *Escherichia coli* Community acquired urinary tract infections: a systematic review. Infect Drug Resist. 2020; 13:3945-55. doi:10.2147/IDR.S269033.

2. Baziboroun M, Bayani M, Poormontaseri Z, Shokri M, Biazar T. Prevalence and antibiotic susceptibility pattern of extended-spectrum beta lactamases producing *Escherichia coli* isolated from outpatients with urinary tract infections in Babol, Northern of Iran. Curr Issues Pharm Med Sci. 2018; 31(2):61-4. doi:10.1515/cipms-2018-0013.

3. Kayastha K, Dhungel B, Karki S, Adhikari B, Banjara MR, Rijal KR, et al. Extended-spectrum β-lactamase-producing *Escherichia coli* and *Klebsiella* species in pediatric patients visiting International Friendship Children's Hospital, Kathmandu, Nepal. Infect Dis (Auckl). 2020; 13:1178633720909798. doi:10.1177/1178633720909798.

4. Chen Y, Liu Z, Zhang Y, Zhang Z, Lei L, Xia Z. Increasing prevalence of ESBL-producing multidrug resistance *Escherichia coli* from diseased pets in Beijing, China from 2012 to 2017. Front Microbiol. 2019; 10:2852. doi:10.3389/fmicb.2019.02852.

5. Ahad A, Salman M, Ikram A, Ashraf Z, Amir A, Saeed A, et al. Prevalence and molecular characterization of ESBL-producing *Escherichia coli* in waste water samples from Pakistan. Int J Infect Dis. 2021; 101(S1):33. doi:10.1016/j.ijid.2020.09.119.

6. Arefinejad A, Khodadadi M, Zeinali T, Yousefi M. Phenotypic and genotypic evaluation of ESBL- and AmpC-producing *Escherichia coli* isolated from chicken distributed in Birjand, East of Iran. Acta Alimentaria. 2023; 52(1):52-60. doi:10.1556/066.2022.00164.

7. Hassuna NA, Khairalla AS, Farahat EM, Hammad AM, Abdel-Fattah M. Molecular characterization of extended-spectrum β lactamase-producing *E. coli* recovered from community-acquired urinary tract infections in Upper Egypt. Sci Rep. 2020; 10(1):2772. doi:10.1038/s41598-020-59772-z.

8. Ugbo EN, Anyamene CO, Moses IB, Iroha IR, Babalola OO, Ukpai EG, et al. Prevalence of blaTEM, blaSHV, and blaCTX-M genes among extended spectrum beta-lactamase-producing *Escherichia coli* and *Klebsiella pneumoniae* of clinical origin. Gene Rep. 2020; 21: 100909. doi:10.1016/j.genrep.2020.100909.

9. Day MJ, Hopkins KL, Wareham DW, Toleman MA, Elviss N, et al. Extended-spectrum β-lactamase-producing *Escherichia coli* in human-derived and foodchain-derived samples from England, Wales, and Scotland: an epidemiological surveillance and typing study. Lancet Infect Dis. 2019; 19(12):1325-35. doi:10.1016/S1473-3099(19)30273-7.

10. Sunarno S, Puspandari N, Fitriana F, Nikmah UA, Idrus HH, Panjaitan NSD. Extended spectrum beta-lactamase (ESBL)-producing *Escherichia coli* and *Klebsiella pneumoniae* in Indonesia and South East Asian countries: GLASS Data 2018. AIMS Microbiol. 2023; 9(2):218-27. doi:10.3934/microbiol.2023013.

11. Ahmed HA, Elsohaby I, Elamin AM, El-Ghafar AEA, Elsaid GA, Elbarbary M, et al. Extended-spectrum β-lactamase-producing *E. coli* from retail meat and workers: genetic diversity, virulotyping, pathotyping and the antimicrobial effect of silver nanoparticles. BMC Microbiol. 2023; 23(1):212. doi:10.1186/s12866-023-02948-0.

12. Prah JK, Amoah S, Ocansey DW, Arthur R, Walker E, Obiri-Yeboah D. Evaluation of urinalysis parameters and antimicrobial susceptibility of uropathogens among out-patients at University of Cape Coast Hospital. Ghana Med J. 2019; 53(1):44-51. doi:10.4314/gmj.v53i1.7.

13. Kettani Halabi M, Lahlou FA, Diawara I, El Adouzi Y, Marnaoui R, Benmessaoud R, et al. Antibiotic resistance pattern of extended spectrum beta lactamase producing *Escherichia coli* isolated from patients with urinary tract infection in Morocco. Front Cell Infect Microbiol. 2021; 11:720701. doi:10.3389/fcimb.2021.720701.

14. Clinical and Laboratory Standards Institute. Performance standards for antimicrobial susceptibility testing. twenty-ninth informational supplement. 2022. Available from: http:////www.clsi.org.

15. Vachvanichsanong P, McNeil EB, Dissaneewate P. Extended-spectrum beta-lactamase *Escherichia coli* and *Klebsiella pneumoniae* urinary tract infections. Epidemiol Infect. 2020; 149:e12. doi:10.1017/S0950268820003015.

16. Shrestha R, Khanal S, Poudel P, Khadayat K, Ghaju S, Bhandari A, et al. Extended spectrum β-lactamase producing uropathogenic *Escherichia coli* and the correlation of biofilm with antibiotics resistance in Nepal. Ann Clin Microbiol Antimicrob. 2019; 18(1):42. doi:10.1186/s12941-019-0340-y.

17. Al-Jamei SA, Albsoul AY, Bakri FG, Al-Bakri AG. Extended-spectrum β-lactamase producing *E. coli* in urinary tract infections: a two-center, cross-sectional study of prevalence, genotypes and risk factors in Amman, Jordan. J Infect Public Health. 2019; 12(1):21-5. doi:10.1016/j.jiph.2018.07.011.

18. Rajabnia M, Forghani MS, Hasani S, Bahadoram M, Mohammadi M, Barahman M. Prevalence and antibiotic resistance pattern of extended-spectrum beta lactamase producing *Escherichia coli* isolated from urinary tract infection. J Renal Inj Prev. 2019; 8(2):78-81. doi:10.15171/jrip.2019.15.

19. Kumar N, Chatterjee K, Deka S, Shankar R, Kalita D. Increased isolation of extended-spectrum beta-lactamase-producing *Escherichia coli* from community-onset urinary tract infection cases in Uttarakhand, India. Cureus. 2021; 13(3):e13837. doi:10.7759/cureus.13837.

20. Abayneh M, Tesfaw G, Abdissa A. Isolation of extended-spectrum β-lactamase- (ESBL-) producing *Escherichia coli* and *Klebsiella pneumoniae* from patients with community-onset urinary tract infections in Jimma University Specialized Hospital, Southwest Ethiopia. Can J Infect Dis Med Microbiol. 2018; 2018:4846159. doi:10.1155/2018/4846159.

21. Besharati Zadeh S, Shakib P, Zolfaghari MR, Farajzadeh Sheikh A. Prevalence of *Escherichia coli* and *Klebsiella pneumoniae*, producing extended-spectrum beta-lactamase (ESBLs) from clinical specimen in Khuzestan, Iran. Gene Cell Tissue. 2021; 8(3):e112377. doi:10.5812/gct.112377.

22. Higuchi H, Nakamura T, Mashino J, Imada T, Morimoto T. Prediction of ESBL-producing *E coli* for suspected urinary tract infection. Urologia. 2023; 90(1):151-6. doi:10.1177/03915603221103438.

23. Ibrahim DR, Dodd CER, Stekel DJ, Meshioye RT, Diggle M, Lister M, et al. Multidrug-resistant ESBL-producing *E. coli* in clinical samples from the UK. Antibiotics (Basel). 2023; 12(1):169. doi:10.3390/antibiotics12010169.

24. Sarker JN, Ali Ahmed SM, Sultana H, Anwar S, Tarafder S, Saleh AA. Antibiogram of extended-spectrum β-lactamase (ESBL) producing *Escherichia coli*. Open J Med Microbiol. 2019; 9(2):41-7. doi:10.4236/ojmm.2019.92006.

25. Gaviria LP, Montsant L, Azuaje C, Gonzalez-Diaz A, Horcajada JP, Limon E, et al. A descriptive analysis of urinary ESBL-producing-*Escherichia coli* in Cerdanya Hospital. Microorganisms. 2022; 10(3):488. doi:10.3390/microorganisms10030488.

Original Article

Comparative Effectiveness and Safety of Levetiracetam and Sodium Valproate in Children with Refractory Status Epilepticus

Asif Javeed, Atif Ashraf, Saba Wamiq, Sidra Anjum, Allah Nawaz Sultan, Nosheen Iftikhar

ABSTRACT

Objective: To compare the safety and efficacy of levetiracetam (LEV) and sodium valproate (SVP) for the treatment of children with refractory status epilepticus (RSE).

Methodology: This cross-sectional study was conducted in the Department of Pediatrics, Nishtar Medical Hospital, Multan from September 2022 to August 2023. A total of 90 children presenting with refractory status epilepticus were included in the study by consecutive sampling technique. The patients were divided into two groups. Group A (n=45) was administered levetiracetam intravenously at 30 mg/kg bolus followed by the same dose 12 hourly. Group B (n=45) was administered sodium valproate intravenously at 20mg/kg, followed by eight hourly doses of 10mg/kg. The treatment was labelled as effective if the seizures were controlled within 30 minutes and then the patient remained symptom-free for 24 hours after treatment initiation. The occurrence of adverse events assessed the safety of the drugs. Data analysis was performed using Statistical Package for the Social Sciences (SPSS) version 20.

Results: The mean age was 5.4±5.1 years and 6.3±5.2 years in groups A and B, respectively. The most common etiological causes were acute symptomatic causes. Encephalitis was found in 14(31.1%) and 25(55.5%) patients in groups A & B. In group A, the seizure was controlled in 33(73.3%) patients within 30 minutes and in group B, the seizure was controlled in 26(57.7%) patients.

Conclusion: Levetiracetam and sodium valproate are equally beneficial in terms of effectiveness & safety for the refractory status epilepticus in children.

Keywords: *Seizures. Status epilepticus. Levetiracetam. Sodium valproate.*

INTRODUCTION

Status epilepticus is a severe neurological disorder that is common in the pediatric population with high morbidity and mortality rates. The drugs commonly used to control this medical emergency are benzodiazepines and phenytoin.[1] However, in 11-43% of cases, the status epilepticus is not controlled with these primary drugs and converts to RSE. Refractory status epilepticus is defined as seizure activity that persists after administration of a first-line benzodiazepine and a second-line antiseizure drug.[2] Recent studies showed that anticonvulsant drugs levetiracetam and sodium valproate could be used before the use of anaesthetic agents to treat RSE in children.[3] Sodium valproate plays a significant role in the treatment of children with RSE as a second-line therapy. It acts on the gamma-aminobutyric acid (GABA) neurotransmitter by blocking specific channels, stabilizing the neurons, and reducing the spread of excitatory signals in the brain. It also helps to prevent seizures. Due to its broader mechanism of action, it can be used to treat RSE in patients who do not respond to initial treatment. However, care must be taken to use this drug as it affects the liver and also lowers the platelet count in children. Despite these considerations, sodium valproate remains an essential tool in managing refractory seizures in children and can lead to better clinical outcomes.[4]

Levetiracetam is a relatively new second-line antiepileptic drug with limited side effects and is safer to use in children. Some of the side effects are behavioral change and aggression.[5]

Comparison of levetiracetam and sodium valproate for the treatment of refractory status epilepticus in children can provide valuable insights into the optimal management of this condition, inform clinical practice, and improve outcomes for pediatric patients. The findings may contribute to the development of evidence-based guidelines and protocols explicitly tailored to the pediatric population. Thus, we conducted this study to compare the safety and efficacy of levetiracetam and sodium valproate for the treatment of children with refractory status epilepticus.

METHODOLOGY

This cross-sectional study was conducted at the Department of Pediatrics, Nishtar Medical Hospital, Multan from September 2022 to August 2023. A total of ninety participants were enrolled in this study. The children diagnosed with refractory status

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epilepticus and aged one month to eighteen years were included in this study by consecutive sampling technique. Children allergic to levetiracetam or sodium valproate, those with epilepsia partialis continua, liver disease, and abnormal inborn metabolism were excluded.

All the children's guardians and parents were informed about the procedure and informed written consent was obtained individually. The study protocols were approved by the ethics committee of the hospital (Letter No. 27/22/NMU, 17-08-2022). The enrolled patients were divided into group A (n=45) and group B (n=45). Group A received intravenous levetiracetam at 30 mg/kg as a bolus followed by the same dose administered every 12 hours. Group B received intravenous sodium valproate at 20 mg/kg followed by 10 mg/kg every 8 hours.

The treatment was labelled as effective if the seizures were controlled within 30 minutes and then the patient remained symptom-free for 24 hours after treatment initiation. The occurrence of adverse events assessed the safety of the drugs. Patient history related to seizures, vital signs, duration of seizure, and treatment outcomes were also noted. All patients were monitored for 24 hours for vital signs and changes in convulsions.

STATISTICAL ANALYSIS

Data analysis was performed using Statistical Package for the Social Sciences (SPSS) version 20. The results were analyzed using a combination of statistical tests to assess differences between group A and group B. Continuous variables such as age, duration of seizure, and average time to control seizure were compared using t-tests, with p-values indicating statistical significance. Categorical variables, including gender, presenting symptoms, etiological causes, response to seizure at 30 minutes and 24 hours, and presence of neurological deficit were analyzed using Chi-square tests to determine significant differences between the two groups. Wilcoxon sum tests were applied for continuous variables with non-normal distributions like protein content in cerebrospinal fluid. A p-value of less than or equal to 0.05 was considered statistically significant.

RESULTS

The mean age of the patients was 5.4±5.1 years in group A and 6.3±5.2 years in group B with no significant difference (p=0.580). Gender distribution was similar with 26(57.8%) males in group A and 28(62.2%) in group B (p=0.819). Presenting symptoms such as fever, headache, rash, diarrhoea, upper respiratory tract infections, vomiting, and jaundice showed no significant differences between the groups. The mean seizure duration in group A was 7.24±1.5 days and in group B, it was 7.7±1.2 days with no significant difference (p=0.909). The seizures (tonic and tonic-clonic) also did not vary significantly between the groups. The insignificant p-value showed that the two groups were comparable in assessing the significance of treatment between the groups.

Table 1 shows the distribution of diagnosis contributing to refractory status epilepticus among the two groups. The diagnosis was categorized into acute symptomatic and remote symptomatic causes. In group A, encephalitis was identified in 14(31.1%) patients, meningitis in 12(26.7%) patients, and intracerebral brain haemorrhage in 6(13.3%) patients. In group B, encephalitis was more prevalent in 25(55.5%) patients, while meningitis was identified in 4(8.8%) patients and intracerebral brain haemorrhage in 2(4.4%) patients. Encephalitis significantly differed between the two groups (p=0.005), indicating a higher incidence in group B. Other conditions did not exhibit statistically significant differences between the groups (Table 1).

Table 2 presents the response of patients to interventions for refractory status epilepticus in group A and group B. At 30 minutes post-intervention, 73.3% of patients in group A and 57.7% in group B showed seizure control, although this difference was not statistically significant (p=0.238). Similarly, at 24 hours, seizure control was achieved in 27(65.8%) patients of group A and 29(67.4%) patients of group B with no significant difference observed between the groups (p=0.867). The average time to control seizures was comparable between the two groups (p=0.439). The proportion of patients who crossed over to the other treatment group was 26.7% in group A and 37.8% in group B (p=0.470), and there was no significant difference in the proportion of patients refractory at 24 hours between the two groups (p=0.710). Additionally, the adverse events such as mortality, neurological deficit, and length of hospital stay did not differ significantly between the groups (Table 2).

DISCUSSION

Refractory status epilepticus is an acute, critical, and severe condition. It has long-term negative effects like neuronal death, damage, and neuronal network change.[6] In this study, the efficacy of sodium valproate and levetiracetam were compared in this critical condition.

Table 1: Etiological Causes of RSE in Study Groups

Diagnosis		Group A (n=45)	Group B (n=45)	p-value
Acute Symptomatic	Encephalitis	14(31.1%)	25(55.5%)	0.005*
	Meningitis	12(26.7%)	4(8.8%)	0.070
	Intracerebral Brain Hemorrhage	6(13.3%)	2(4.4%)	0.200
	Drowning	0(0%)	2(4.4%)	0.460
	Hypernatremia	3(6.6%)	0(0%)	0.499
	Hypocalcemia	3(6.6%)	2(4.4%)	0.599
Febrile Seizure		0(0%)	2(4.4%)	0.969
Remote Symptomatic	Cerebral Palsy	3(6.6%)	4(8.8%)	0.550
	Hydrocephalus	0(0%)	2(4.4%)	0.568
	Sturge-Weber Syndrome	0(0%)	2(4.4%)	0.866
	Corpus Collosum Agenesis	0(0%)	2(4.4%)	0.964
	Brain Tumour	0(0%)	2(4.4%)	0.789
	Inborn Errors of Metabolism	2(4.4%)	2(4.4%)	0.655
Idiopathic		5(11.1%)	4(8.8%)	0.749

**Significant p-value*

Table 2: Efficacy and Safety of Levetiracetam & Sodium Valproate

Response to Seizure		Group A	Group B	p-value
At 30 Min	Number of Patients	45	45	
	Controlled	33(73.3%)	26(57.7%)	0.238
	Uncontrolled	12(26.7%)	19(42.3%)	
At 24 Hours	Number of Patients	41	43	0.867
	Controlled	27(65.8%)	29(67.4%)	
	Uncontrolled	14(34.2%)	14(32.6%)	
	Average Time to Control Seizure (min)	34.57±17.93	38.37±20.84	0.439
	Crossed Over Patients	12(26.7%)	17(37.8%)	0.470
	Crossed Over Patients' Refractory at 24 Hours	6(13.3%)	9(20%)	0.710
	Death	14(31.1%)	12(26.7%)	0.505
	Duration of Hospital Stay (Days)	7.48±5.01	8.81±6.6	0.257
After One Month	Number of Patients	22	30	0.954
	Seizure Controlled	17(77.3%)	25(83.3%)	0.225
	Neurological Deficit	5(22.7%)	5(16.7%)	0.318

The mean age in groups A and B was 5.4±5.1 years and 6.3±5.2 years, respectively. Twenty six (57.8%) patients in group A and 28(62.2%) in group B were males. The age and gender ratio were similar to previous data.[7] Our results showed a mean duration of seizures of 7.24±1.5 days in group A & 7.7±1.2 days in group B with no significant difference (p=0.909). Similar results were found in another study.[6]

In our study, the most common causes of RSE were acute symptomatic, in which encephalitis was the most common followed by meningitis and intracerebral brain haemorrhage. This is similar to the etiological profile reported by Chu et al. This review article also showed that the most common causes of RSE reported by the previous studies were encephalitis and meningitis.[8]

Our results showed that in 33(73.3%) patients seizures were controlled by levetiracetam, whereas in 26(57.7%) patients seizures were controlled by SVP after 30 minutes. No significant difference was found between the groups (p-value=0.238). A similar study was conducted by Nene et al. to assess the efficacy of SVP and LEV in managing pediatric status epilepticus. The study showed treatment with SVP controlled seizures in 68.3% and 74.1% of LEV groups. Upon completion of the study after 24 hours, seizure control rates were 76% in the SVP group and 86% in the LEV group. However, no statistically significant difference was noted.[9]

In another study, phenytoin, SVP, and LEV were compared and no statistically significant difference in controlling RSE was found. The average time to

control seizure was 34.57±17.93 minutes in group A and 38.37±20.84 minutes in group B.[10]

However, another study showed controlled seizures in 68.1% of patients after administering levetiracetam.[11] Another survey conducted in the pediatric population of partial seizures reported a success rate of 52% in a group given levetiracetam intravenously which is less than our study.[12] Nazir et al. conducted a study on antiepileptic drugs, and their results showed at 24 hours, seizures were controlled in 44(88%) patients in the phenytoin group, 39(78%) patients in the levetiracetam group and 46 patients (92%) in valproate group with insignificant p-value (p=0.115).[13] Similar to the results of our study where insignificant results were noted in both groups.

Another study conducted by Arican et al. included 92 patients, 61(66%) patients were seizure-free free and 34% still experiencing seizures after 72 hours of administration of the levetiracetam. This study emphasized that early control of seizures positively affects their long-term control.[14]

In our study, the high mortality rate was 28.9% which can be justified by the presence of acute symptomatic diseases and delay in treatment compared to the previous study, reporting a lower mortality rate of 7.6%.[8]

A systematic review and meta-analysis concluded that levetiracetam is not superior to valproate in terms of safety and efficacy outcomes. Moreover, the responses to LEV and valproate in children (under 18 years) and adults (over 18 years) were similar.[15]

CONCLUSION

Levetiracetam and sodium valproate are equally beneficial in terms of effectiveness & safety for the refractory status epilepticus in children.

LIMITATIONS & RECOMMENDATIONS

The study has limitations, including a small sample size of 90 children, a single-centered design, and a short follow-up duration, potentially limiting generalizability and comprehensive outcome assessment. Based on the study's findings, it is recommended to consider both levetiracetam and sodium valproate as viable treatment options for refractory status epilepticus in children. Additionally, future research should explore individual patient characteristics and etiological factors to personalize treatment approaches and optimize outcomes in pediatric patients with refractory status epilepticus.

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Authors' Contributions:

A.J: Study design
A.A: Drafting of manuscript
S.W: Data Analysis and Results write up
S.A: Data collection and write-up methodology
A.N.S: Literature review and drafting
N.I: Proofreading and final approval

REFERENCES

1. Messahel S, Bracken L, Appleton R. Optimal management of status epilepticus in children in the emergency setting: a review of recent advances. Open Access Emerg Med. 2022; 14:491-506. doi:10.2147/OAEM.S293258.

2. Vasquez A, Farias-Moeller R, Tatum W. Pediatric refractory and super-refractory status epilepticus. Seizure. 2019; 68:62-71. doi:10.1016/j.seizure.2018.05.012

3. Xue T, Wei L, Shen X, Wang Z, Chen Z, Wang Z. Levetiracetam versus phenytoin for the pharmacotherapy of benzodiazepine-refractory status epilepticus: a systematic review and meta-Analysis of randomized controlled trials. CNS Drugs. 2020; 34(12):1205-1215. doi: 10.1007/s40263-020-00770-0.

4. Liampas I, Siokas V, Brotis A, Zintzaras E, Stefanidis I, Dardiotis E. Intravenous sodium valproate in status epilepticus: review and meta-analysis. Int J Neurosci. 2021; 131(1):70-84. doi:10.1080/00207454.2020.1732967.

5. Nalisetty S, Kandasamy S, Sridharan B, Vijayakumar V, Sangaralingam T, Krishnamoorthi N. Clinical effectiveness of levetiracetam compared to fosphenytoin in the treatment of benzodiazepine refractory convulsive status epilepticus. Indian J Pediatr. 2020; 87(7):512-9. doi:10.1007/s12098-020-03221-2.

6. Wu H, Liu J, Qian F, Yang J, Wang Y, Guan S. Clinical Evaluation of Levetiracetam in the Treatment of Epilepsy. J Healthc Eng. 2022 Apr 5;2022:3789516. doi: 10.1155/ 2022/3789516.

7. DeMott JM, Slocum GW, Gottlieb M, Peksa GD. Levetiracetam vs. phenytoin as 2nd-line treatment for status epilepticus: a systematic review and meta-analysis. Epilepsy Behav. 2020; 111:107286. doi:10.1016/j.yebeh. 2020.107286.

8. Chu SS, Wang HJ, Zhu LN, Xu D, Wang XP, Liu L. Therapeutic effect of intravenous levetiracetam in status epilepticus: a meta-analysis and systematic review. Seizure. 2020; 74:49-55. doi:10.1016/j.seizure.2019.11.007.

9. Nene D, Mundlamuri RC, Satishchandra P, Prathyusha PV, Nagappa M, Bindu PS, et al. Comparing the efficacy of sodium valproate and levetiracetam following initial lorazepam in elderly patients with generalized convulsive status epilepticus (GCSE): a prospective randomized controlled pilot study. Seizure. 2019; 65:111-7. doi:10.1016/j.seizure.2019.01.015.

10. Vignesh V, Rameshkumar R, Mahadevan S. Comparison of phenytoin, valproate and levetiracetam in pediatric convulsive status epilepticus: a randomized double-blind controlled clinical trial. Indian Pediatr. 2020; 57(3):222-7. doi:10.1007/s13312-020-1755-4.

11. Kapur J, Elm J, Chamberlain JM, Barsan W, Cloyd J, Lowenstein D, et al. Randomized trial of three anticonvulsant medications for status epilepticus. N Engl J Med. 2019; 381(22):2103-13. doi:10.1056/NEJMoa 1905795.

12. Cao Y, He X, Zhao L, He Y, Wang S, Zhang T, et al. Efficacy and safety of levetiracetam as adjunctive treatment in children with focal onset seizures: a systematic review and meta-analysis. Epilepsy Res. 2019;153:40-8. doi:10.1016/j.eplepsyres.2019.04.001.

13. Nazir M, Tarray RA, Asimi R, Syed WA. Comparative efficacy of IV phenytoin, IV valproate, and IV levetiracetam in childhood status epilepticus. Journal of Epilepsy Research. 2020 Dec;10(2):69.doi: 10.14581/ jer.20011.

14. Arican P, Gencpinar P, Cavusoglu D, Olgac Dundar N. Levetiracetam monotherapy for the treatment of infants with epilepsy. Seizure. 2018; 56:73-7. doi:10.1016/j. seizure.2018.02.006.

15. . Wang S, Wu X, Xue T, Song Z, Tan X, Sun X, Wang Z. Efficacy and safety of levetiracetam versus valproate in patients with established status epilepticus: A systematic review and meta-analysis. Heliyon. 2023 Feb 1;9(2):e13380. doi: 10.1016/j.heliyon.2023.e13380.

Original Article

Diagnostic Accuracy of Intravenous Urography for Detection of Urinary Tract Calculi taking Unenhanced Computed Tomography as Gold Standard

Abdullah Ali Adnan, Muhammad Saleem Akhter

ABSTRACT

Objective: To determine the diagnostic accuracy of intravenous urography (IVU) for the detection of urinary tract calculi taking unenhanced computed tomography (CT) as gold standard**.**

Methodology: This descriptive cross-sectional study was conducted at the Department of Radiology, Sahiwal Teaching Hospital, Sahiwal from June to November 2021 after ethical approval. Two hundred and forty patients between 16-85 years of age with signs and symptoms of urolithiasis were included after taking informed consent. Non-probability convenient sampling technique was used. Patients with renal function impairment, history of urolithiasis in the last 6 months, on peritoneal dialysis, pregnant females, or allergic to contrast medium were excluded. Intravenous urography and then unenhanced CT of the kidney, ureter & bladder (CT-KUB) were performed on all patients to diagnose renal stones. The findings of both modalities were compared. Data was analyzed through Statistical Package of the Social Sciences (SPSS) version 25. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and diagnostic accuracy of IVU were calculated taking CT-KUB as gold standard.

Results: Among 240 subjects, IVU detected the urinary tract calculi in 125(52.1%) patients with sensitivity and specificity of 94.26% and 91.52%, respectively. The diagnostic accuracy of IVU was found to be 92.90% in diagnosing urolithiasis keeping unenhanced CT as gold standard.

Conclusion: Intravenous urography is a simple, economical, and easily available imaging modality for the detection of urinary tract calculi. It can be applied routinely for detecting urinary tract calculi.

Keywords: *Urolithiasis. Renal colic. Sensitivity. Specificity.*

INTRODUCTION

Urinary tract calculi or urolithiasis occurs as a result of the crystallization of solutes in urine. Many factors contribute in the formation of stones in the urinary tract such as anatomic variations, decreased volume of urine, high oxalate or high sodium diet, certain medications, infections of the urinary tract, and genetic factors such as cystinuria.[1] Urolithiasis is a highly prevalent disease worldwide. Also, it is the cause of end-stage renal disease in 4-8% of the patients.[2] The symptoms of urolithiasis depend on their location in the urinary tract i.e. kidney, ureter,or urinary bladder. Common symptoms include flank or lumbar pain, hematuria, decreased urinary flow, urinary obstruction, or infection of the urinary tract. Bladder stones can present with recurrent urinary tract infections.[3]

For the timely diagnosis and appropriate management of urolithiasis, various imaging modalities can be used such as ultrasound kidney, ureter & bladder (KUB), intravenous urography (IVU)/intravenous pyelogram (IVP), CT-KUB, and magnetic resonance imaging (MRI). Among these, CT-KUB has been considered a modality of choice.[4] Unenhanced CT has been thought as the right modality as it takes less time and there is no risk of contrast reaction. Moreover, the density and nature of calculus can be determined. It can locate the exact site of the calculus as well. It has been consideredas gold standard modality with high sensitivity and specificity although it poses a high risk of radiation.[5] Urinary tract calculi can also be detected efficiently using IVU. Intravenous urography has been widely used in the detection of suspected urolithiasis as well as the functional status of kidneys. The urinary tract can be well assessed with IVU including both kidneys, ureters, and urinary bladder.[5]

This study was planned to determine the diagnostic accuracy of IVU to diagnose urolithiasis considering unenhanced CT-KUB as gold standard. The results of the study will help us in using IVU as a diagnostic modality for urolithiasis.

METHODOLOGY

This descriptive cross-sectional study was conducted at the Department of Radiology, Sahiwal Teaching Hospital, Sahiwal from June to November 2021. A sample size of 240 cases was calculated with a 95% confidence level and 5% margin of error, taking the prevalence of ureteric calculi as 21.1% and the sensitivity of IVU at 85%.[4,6] After taking permission

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from the ethical review committee (Letter No: 57-A/SLMC/SWL, 23-10-2020), sampling was done by non-probability convenient sampling technique. The study included 240 patients of age 16-85 years of either gender presenting with signs and symptoms of urolithiasis. Patients with renal function impairment, history of urolithiasis in the last 6 months, on peritoneal dialysis, pregnant females, or allergic to contrast medium (on medical record) were excluded. Informed consent was taken. Intravenous urography was performed by Optima DRF Apelem Fluoroscopy Unit. Plain abdominal film was taken before intravenous administration of 50 mL of non-ionic contrast medium, followed by an anteroposterior view at 5 minutes, anteroposterior and bilateral oblique views at 15 min, anteroposterior view at 30 min, and a post-voiding view. Reports were assessed and the presence of renal stones was noted. After 3 days of IVU, patients were sent for CT-KUB. All images were obtained with a helical scanner (bright speed, 128 slice, GE scanner) without intravenous or oral contrast. The presence or absence of stone was confirmed by CT-KUB.

STATISTICAL ANALYSIS

All the collected data was entered and analyzed through the Statistical Package for the Social Sciences (SPSS) version 25. Quantitative data was presented as mean±SD. Qualitative variables were presented as frequency and percentage. Sensitivity, specificity, PPV, NPV, and diagnostic accuracy of IVU were calculated taking CT-KUB as gold standard.

RESULTS

A total of 240 patients with a mean age of 43.10±8.27 years and an age range of 16-85 years were included in this study. One hundred and ninety four (80.8%) patients were between 51-85 years, while 46(19.2%) patients fell between 16-50 years of age.

Among 240 patients, 139(57.9%) were female and 101(42.1%) were male with a female-to-male ratio of 1.4:1. Intravenous urography confirmed the diagnosis of urinary tract calculi in 125(52.1%) patients. Out of 240, CT-KUB diagnosed 122 (50.8%) cases (Table 1). The sensitivity, specificity, positive predictive value, and negative predictive value of IVU for the detection of urinary tract calculi taking unenhanced computed tomography as gold standard were found to be 94.26%, 91.52%, 92.01%, and 93.91%, respectively. The diagnostic accuracy of IVU was 92.90% which was found to be statistically significant for the diagnosis of urolithiasis (p-value=0.0001) (Table 2).

Table 1: Results of IVU and CT-KUB for Detection of Urinary Tract Calculi

IVU	CT-KUB		Total	p-value
	Positive	Negative		
Positive	115(47.9%) (TP)	10(4.2%) (FP)	125(52.1%)	0.0001*
Negative	7(2.9%) (FN)	108(45%) (TN)	115(47.9)	
Total	122(50.8%)	118(49.2%)	240(100%)	

**Significant p-value*

Table 2: Parameters of Diagnostic Accuracy of IVU and CT-KUB

Diagnostic Parameters	IVU	CT-KUB
Sensitivity	94.26%	92.0%
Specificity	91.52%	93.9%
Positive Predictive Value	92.01%	94.2%
Negative Predictive Value	93.91%	91.5%
Diagnostic Accuracy	92.90%	92.9%

DISCUSSION

Urolithiasis can cause severe complications including chronic renal disease and infections. So, its proper diagnosis & management is very important to improve outcomes of the patients.[7] Intravenous urography is a significant diagnostic modality to assess pathologies of kidneys, ureters, and urinary bladder.[8] It is found to be one of the minimally invasive procedures that aid in accurate diagnosis.[9]

Our results demonstrated the mean age of participants to be 43.10±8.27 years and the majority of cases presented with urolithiasis were between 51-85 years of age. The prevalence of urolithiasis among females was higher (57.9%) than that of males. Another study conducted in Iran by Moftakhar et al. found that the mean age of the study

population was 52.15±8.22 years. They found a higher prevalence of urolithiasis in females with a female-to-male ratio of 1.25:1. Moreover, the prevalence of urolithiasis was higher in middle age group in both genders.[6] According to another study, the prevalence of urinary tract calculi was high in females and this increasing trend was attributed to obesity and eating habits.[10] A review conducted by Gillams et al. showed increasing trends of prevalence of urolithiasis among females, whereas the prevalence of urolithiasis among males is static over a period of 10 years.[11] On the other hand, a study conducted by Wang et al. showed high prevalence of urolithiasis in males during 50-59 years and in females during 60-69 years.[12] Similarly, another study found that the males are more affected with ureteric calculi (51.7%) as compared to females (48.3%).[13]

Intravenous urography is easily available, cost-effective, and has been used widely to detect urinary tract calculi in addition to the functional status of kidneys.[14] Our study showed the presence of urinary tract calculi in 125(52.1%) patients on IVU. The sensitivity, specificity, positive predictive value, and negative predictive value of IVU for the detection of urinary tract calculi were found to be 94.26%, 91.52%, 92.01%, and 93.91%, respectively in our study. The diagnostic accuracy of IVU was 92.90%. A study done by Jana et al. depicted that IVU correctly identified urolithiasis in 78.7% of the patients. They found sensitivity, specificity, and diagnostic accuracy of IVU as 75%, 95.12%, and 88.52%, respectively.[15]

Another prospective study was conducted to compare CT-KUB and IVU. It was reported that IVU had sensitivity of 85.2% and specificity of 90.4%, whereas the sensitivity and specificity of CT-KUB were 94.1% and 94.2%, respectively. They also documented that IVU can be used where anatomical identification remains a big challenge.[4] On the contrary, a study by Sabharwal et al. showed that non-contrast CT had higher rate of detection of urinary tract calculi as compared to IVU, 63.3% versus 51.3% cases, respectively.[16]

Another study reported poor diagnostic parameters of IVU as compared to CT-KUB. The sensitivity, specificity, PPV, and NPV of IVU were 72.08%, 91.67%, 95.56%, and 57.89%, respectively and its diagnostic accuracy was 78.31%. However, CT-KUB had sensitivity of 96.61%, specificity of 95.83%, PPV of 98.28%, NPV of 92.00%, and diagnostic accuracy of 96.39%.[17]

A study by Sheikh et al. showed that IVU accurately detected urolithiasis in 40.5%, while CT detected urolithiasis in 42% of the patients. The diagnostic accuracy of IVU was found to be 94%.[18]

Another study reported that IVP can diagnose urinary tract calculi. Furthermore, it can determine the location, degree of obstruction, and functional status of kidneys.[8]

CONCLUSION

Our study showed high diagnostic accuracy of IVU for the diagnosis of urolithiasis. Intravenous urography is a simple reliable, economical, and easily available imaging modality for the detection of urinary tract calculi. It can be applied routinely for detecting urinary tract calculi.

LIMITATIONS & RECOMMENDATIONS

The small sample size was one of the limitations of our study. We recommend that this simple, economical, and easily available imaging modality should be applied routinely in every patient with ureteric colic for detecting ureteric calculi. Further studies recruiting a large number of subjects in this region are needed.

Conflict of Interest: None.
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Authors' Contributions:
A.A.A: Concept of the study, Drafting, Collection of data
M.S.A: Concept of the study, Drafting, Statistical Analysis, Final Approval

REFERENCES

1. Shastri S, Patel J, Sambandam KK, Lederer ED. Kidney stone pathophysiology, evaluation and management: core curriculum 2023. Am J Kidney Dis. 2023; 82(5):617-34. doi:10.1053/j.ajkd.2023.03.017.
2. Borumandnia N, Fattahi P, Talebi A, Taheri M, Alvani MS, Balani MM, et al. Longitudinal trend of urolithiasis incidence rates among world countries during past decades. BMC Urol. 2023; 23(1):166. doi:10.1186/s12894-023-01336-0.
3. Akram M, Jahrreiss V, Skolarikos A, Geraghty R, Tzelves L, Emilliani E, et al. Urological guidelines for kidney stones: overview and comprehensive update. J Clin Med. 2024; 13(4):1114. doi:10.3390/jcm13041114.
4. Al-Shawi MM, Aljama NA, Aljedani R, Alsaleh MH, Atyia N, Alsedrah A, et al. The role of radiological imaging in the diagnosis and treatment of urolithiasis: a narrative review. Cureus. 2022; 14(12):e33041. doi:10.7759/cureus.33041.

5. Faidah S, Banjar A, Zarbah J, Alfaer S, Alshulayyil M, Alsalami S, et al. Contrast versus non-contrast CT in urinary tract calculi. Int J Community Med Public Health. 2018; 5(3):818-21. doi:10.18203/2394-6040.ijcmph 20180417.

6. Moftakhar L, Jafari F, Ghoddusi Johari M, Rezaeianzadeh R, Hosseini SV, Rezaianzadeh A. Prevalence and risk factors of kidney stone disease in population aged 40-70 years old in Kharameh cohort study: a cross-sectional population-based study in southern Iran. BMC Urol. 2022; 22(1):205. doi:10.1186/s12894-022-01161-x.

7. Almaghlouth AK, Alqutayfi HM, Bohamad AH, Almarzooq AJ, Alamer MA, Alqattan DJ. Urolithiasis symptoms and risk factors among the general population of Alahsa, Saudi Arabia. Cureus. 2023; 15(5):e39645. doi:10.7759/cureus.39645.

8. Mehta SR, Annamaraju P. Intravenous Pyelogram. StatPearls. Available from: https://www.ncbi.nlm.nih.gov/books/NBK559034/

9. Huang C, Luo X, Wang S, Wan YU, Wang J, Tang X, et al. Minimally invasive cytopathology and accurate diagnosis: technical procedures and ancillary techniques. In Vivo. 2023 Jan-Feb;37(1):11-21. doi: 10.21873/invivo.13050.

10. Cicerello E, Mangano MS, Cova G, Ciaccia M. Changing in gender prevalence of nephrolithiasis. Urologia. 2021; 88(2):90-3. doi:10.1177/0391560320966206.

11. Gillams K, Juliebo-Jones P, Juliebo SO, Somani BK. Gender differences in kidney stone disease (KSD): findings from a systematic review. Curr Urol Rep. 2021; 22(10):50. doi:10.1007/s11934-021-01066-6.

12. Wang S, Zhang Y, Zhang X, Tang Y, Li J. Upper urinary tract stone compositions: the role of age and gender. Int Braz J Urol. 2020; 46(1):70-80. doi:10.1590/S1677-5538.IBJU.2019.0278.

13. Memon S, Sahito AA, Suhail MA, Ashraf A, Kumari S, Ali K. Diagnostic accuracy of ultrasound in detection of ureteric calculi taking CT KUB as gold standard. PJMHS. 2021; 15(04):1349-51. Available from: https://pjmhsonline.com/2021/april/1349.pdf.

14. Khalid S, Aslam N, Bashir S, Waseem H. Risk factors of renal stones among adult patients visiting tertiary care hospitals, Lahore. LGULS. 2020; 4(03):200-8. doi:10.54692/lgujls.2020.0403110.

15. Jana S, Ghosh SK. Comparison of computed tomography urography and sonographically tailored intravenous urography in patients of urolithiasis. IOSR-JDMS. 2019; 18(3):57-60. doi:10.9790/0853-1803055760.

16. Sabharwal S, Sharma P, Mahajan M. Non-Contrast computed tomography versus intravenous pyelography in the diagnosis of urolithiasis and urinary tract obstruction: a prospective study. GJRA. 2019; 8(2):34-5. Available from: https://www.worldwidejournals.com/global-journal-for-research-analysis-GJRA/fileview/February_2019_1549360633 __92.pdf.

17. Imran F, Zaman Z, Iqbal MJ. Diagnostic accuracy of IVU compared to unenhanced CT KUB for detection of urinary tract calculi. JIMDC. 2017; 6(4):234-9. Available from: https://jimdc.org.pk/index.php/JIMDC/article/view/114/88.

18. Sheikh R, Taqweem ul Haq Q, Abdullah U. Diagnostic role of ultrasonography and X-ray combined versus intravenous urography in evaluation of renal colic. Professional Med J. 2021; 28(05):725-30. doi:10.29309/TPMJ/2021.28.05.5784.

Original Article

Outcomes of Lateral Pancreaticojejunostomy in Patients with Chronic Pancreatitis

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ABSTRACT

Objective: To determine the outcomes of lateral pancreaticojejunostomy (LPJ) in patients with chronic pancreatitis in terms of pain score, opioid use & quality of life (QoL).

Methodology: This descriptive cross-sectional study was conducted at the Department of General Surgery of Peshawar Medical College Group of Hospitals from September 2021 to August 2023. A total of 64 patients were included by non-probability convenient sampling technique. The patients who underwent lateral pancreaticojejunostomy (Partington-Rochelle procedure) for chronic pancreatitis were included. Preoperative and postoperative pain score, use of opioid analgesics, and QoL were noted. The pain score was calculated on the visual analog scale (VAS). The WHO Quality of Life Brief Version (WHOQOL-BREF) questionnaire was used to assess the quality of life in patients above 18 years of age. The pediatric quality of life inventory was used to assess the quality of life in patients below 18 years of age. Statistical Package for the Social Sciences (SPSS) version 25 was used for data analysis.

Results: The mean age of the patients was 19.42±9.12 years. The mean preoperative pain score was 8.13±1.06, while postoperatively it was 1.48±1.40. Preoperatively, 44(68.8%) patients were taking opioid analgesic for pain control, while postoperatively 9(14.1%) patients required opioid analgesics at 8 weeks follow-up. A significant difference was found regarding pain score and opioid analgesic use (p=0.001). The mean preoperative QoL score was 30±15, whereas the mean postoperative score of the QoL scale was 65.23±17.40. The QoL score determined a substantial improvement from a preoperative score to a postoperative score (p=0.001).

Conclusion: Lateral pancreaticojejunostomy for chronic pancreatitis results in significant improvement in quality of life, resolution of abdominal pain, and reduction in opioid consumption with low morbidity and mortality in these patients.

Keywords: *Chronic pancreatitis. Quality of life. Opioid analgesics.*

INTRODUCTION

Chronic pancreatitis is defined as a progressive pathological fibroinflammatory disorder of the pancreas associated with genetic & environmental risk factors. The point prevalence of chronic pancreatitis was 0.045% in the year 2021 with 0.055% and 0.035% in the male and female population.[1] Approximately 50 out of 100,000 population suffer from chronic pancreatitis in the United States.[2] Progressive and repeated inflammation damages pancreatic parenchyma and leads to permanent damage of the pancreas, resulting ultimately in deranged pancreatic enzymes and hormone levels.[3]

Chronic unbearable abdominal pain which is difficult to manage, is the most common presentation of patients with chronic pancreatitis. Chronic pancreatitis is a chronic disorder and it has a negative impact on quality of life.[4] Management commences with lifestyle & dietary modification, and avoidance of smoking and alcohol which are the major risk factors for pancreatitis.[5] Medical treatment includes different types of analgesics for pain control and replacement of pancreatic enzymes. Eventually, these treatment options are not effective in 50-60% of patients and warrant some sort of invasive intervention such as endoscopy or surgery.[6] Intervention such as endoscopy or surgery is mostly indicated for the management of intractable pain abdomen in chronic pancreatitis. Endoscopic interventions are less effective than surgical interventions in chronic pancreatitis.[7]

Surgical procedures devised for chronic pancreatitis are either a parenchymal resection procedure, decompression of the main pancreatic duct, or a combination of both.[8] The most commonly performed decompressive procedure is lateral pancreaticojejunostomy which has evolved over the last 60 years.[9] The Partington-Rochelle modification of the Puestow procedure has emerged as the decompressive procedure of choice for many surgeons over the years.[10]

As lateral pancreaticojejunostomy (Partington-Rochelle procedure) is not performed very frequently and there is little documentation in the literature, particularly regarding the outcomes of the procedure. The purpose of the study was to determine the outcome of lateral pancreaticojejunostomy in patients suffering from chronic pancreatitis with reference to pain score, opioid analgesic use, and quality of life.

METHODOLOGY

This cross-sectional study was conducted at the Department of General Surgery of Peshawar

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Medical College Group of Hospitals i.e. Prime Teaching Hospital and Kuwait Teaching Hospital, Peshawar. The duration of the study was two years from September 2021 to August 2023. Sample size of 64 was calculated using the WHO sample size calculator. After taking approval from the institution review board (Letter No. Prime/IRB/2021-1010, 31-08-2021) patients who presented with chronic pancreatitis were recruited through non-probability convenient sampling technique. The patients who underwent lateral pancreaticojejunostomy (Partington-Rochelle procedure) for chronic pancreatitis were included in this study. Information regarding age, gender, preoperative symptoms including abdominal pain, preoperative treatment & opioid or other analgesics, and preoperative quality of life was collected on the proforma. The postoperative QoL score, pain score & use of opioid or other analgesics were assessed at 8 weeks after the procedure. The pain score was calculated on the visual analog scale. The WHOQOL-BREF questionnaire was used to assess the quality of life in patients above 18 years of age.[11] The pediatric quality of life inventory was used to assess the quality of life in patients below 18 years of age.[12] Cut-off value of quality of life scale was set at 60 or above. The scores were then transformed linearly to a 0-100 scale.

STATISTICAL ANALYSIS

The Statistical Package for the Social Sciences (SPSS) version 25 was used for data analysis. Quantitative variables like age, mean length of hospital stay, and QoL scale were expressed as mean±standard deviation (SD). Qualitative variables such as gender and use of opioid analgesics were expressed as frequencies & percentages. Paired t-test was applied for preoperative & postoperative mean pain scores & QoL scores. Chi-square test was used to compare preoperative and postoperative opioid analgesic use. A p-value of ≤0.05 is taken as significant.

RESULTS

Out of total of 64 patients, 44(68.8%) were male and 20(31.2%) female patients. The mean age of the patients was 19.42±9.12 years, maximum and minimum ages were 44 years and 3 years, respectively. Fifty one (79.7%) patients had intractable abdominal pain. Most of the patients (82.8%) had received symptomatic treatment. These results are shown in Table 1.

The mean length of stay (LOS) was 4.70±1.86 days, maximum and minimum LOS were 12 days and 3 days, respectively. The mean preoperative pain score on the VAS was 8.13±1.06, maximum and minimum scores were 10 and 6, respectively. The mean pain score at 8 weeks follow-up was 1.48±1.40, maximum and minimum pain scores were 5 and 0, respectively. A significant difference was found on the comparison of preoperative & postoperative pain scores (p-value=0.001).

Preoperatively, 44(68.8%) were taking opioid analgesic for pain control, while postoperatively 9(14.1%) patients required opioid analgesics at 8 weeks follow-up with a statistically significant difference (p-value=0.001). Out of the remaining 55(85.9%) patients, 50(78.1%) did not require any analgesic at 8 weeks follow-up and 5(7.8%) were taking non-steroidal anti-inflammatory drugs (NSAIDs) for pain control. The mean preoperative QoL score was 30±15, whereas the mean postoperative QoL score was 65.23±17.40 with a minimum score of 12.50 and maximum of 87.50 at 8 weeks follow-up. The QoL score determined a substantial improvement from a preoperative score to a postoperative score (p=0.001). This indicates a statistically significant enhancement in patients' quality of life following the intervention (Table 2).

Table 1: Study Variables of the Patients

Study Variables		Descriptive Statistics
Age (Years)	**Mean±SD**	19.42±9.12
Gender	**Male**	44(68.8%)
	Female	20(31.2%)
Clinical Manifestations	**Pain**	51(79.7%)
	Exocrine Insufficiency	12(18.7%)
	Bleeding Per Rectum	1(1.6%)
Treatment Received (Before Surgery)	**Symptomatic Treatment**	53(82.8%)
	Endoscopic Retrograde Cholangiopancreatography (ERCP) plus Stenting	10(15.6%)
	Celiac Axis Block	1(1.6%)

Table 2: Comparison of Preoperative and Postoperative Variables

Variables		Preoperative	Postoperative	p-value
Pain Score	**Mean±SD**	8.13±1.06	1.48±1.40	0.001*
Opioid Analgesics Use	**Frequency & Percentage**	44(68.8%)	9(14.1%)	0.001*
QoL Score	**Mean±SD**	30±15	65.23±17.40	0.001*

**Significant p-value*

DISCUSSION

Lateral pancreaticojejunostomy has shown remarkable results in the management of chronic pancreatitis. It has proved to be beneficial in managing intractable chronic abdominal pain, acute exacerbations of pain, and failure of non-invasive or less invasive procedures such as ERCP with stenting.[13] In our study, the mean age of patients was 19.42±9.12 years. Forty four (68.8%) patients were males and 20(31.2%) were females. Out of 64, 51(79.7%) patients presented with abdominal pain. The mean length of stay was 4.70±1.86 days. Preoperative mean pain score on visual analog was 8.13±1.06, whereas it was 1.48±1.40 postoperatively and only 9(14.1%) patients required opioids postoperatively. Fifty (78.1%) patients didn't require any analgesic at 8 weeks follow-up. The mean QoL score was 30±15 preoperatively, while it was 65.23±17.40 postoperatively at 8 weeks follow-up. In a study by Rege et al., a total of 62 patients going through LPJ were included. The mean age of the cohort was 41 years and 37(59.7%) patients were male. Pain was completely relieved in 48(77.4%) patients at one year follow-up.[14] Islam et al. studied 32 cases of chronic pancreatitis of which 27(84.3%) got complete recovery from pain. Among the rest of the five patients, 2 showed reoccurrence of preoperative symptoms and 3 died due to the development of postoperative complications. Overall pain-free survival rate was 84%, while recurrence rate was 6%.[15]

In another study, Baste et al. studied the clinical outcomes of lateral pancreaticojejunostomy in 43 patients of chronic pancreatitis and observed improvement postoperatively. The preoperative mean pain score among all 43 patients was found to be 5.2, indicating moderate pain, while the mean pain scores postoperatively at 15 days, 30 days, and 3 months were 2.54, 2.28, and 0.14, respectively. These results showed significant improvement in pain after the procedure.[16]

According to Hodgman et al., 60% of the patients with chronic pancreatitis had symptomatic improvement of abdominal pain after lateral pancreaticojejunostomy.[17]

Another study included 66 patients of chronic pancreatitis to evaluate the outcome of LPJ. Twenty six (39.4%) patients were free of pain at the 3 year follow-up. Thirty four (51.5%) patients were opioid users at follow-up.[18]

Our study showed a significant improvement in the quality of life after LPJ compared to the pre-surgical score. These results are in line with the previously published study by Pakosz-Golanowska et al. stating that the QoL improved significantly after surgery as is indicated by the Karnofsky index which increased significantly from a mean of 52% (40-70%) before surgery to 82% (70-90%) following surgery.[19] Our study was also supported by research published by Waage et al. with a marked postoperative improvement in QoL.[20] In contrast, Kalady et al. found a significantly lower long-term quality of life improvement at follow-up after surgery.[21]

Another case study on LPJ done in India showed significant improvement in quality of life post-surgery.[22]

Varshney et al. reported that LPJ resulted in better postoperative outcomes in terms of improved QoL & no requirement of oral analgesics.[23] According to other studies, LPJ is a selected treatment that is linked to a lower risk of morbidity and long-term pain alleviation in patients with symptoms of chronic pancreatitis.[24,25] Nag et al. included 24 patients with chronic pancreatitis undergoing LPJ. Out of 24, 13(54%) were males and 11(46%) were females. According to them, there was a significant decrease in the pain score of the patients. Out of 24 patients, excellent outcomes were seen in 17(70.8%) with no recurrence of pain, good in 6(25%) with required enzyme supplementation & NSAIDs occasionally, and fair in 1(4.2%) of the patients who required regular enzyme supplementation and NSAIDs. They concluded that LPJ is a feasible & safe technique in patients with chronic pancreatitis.[26]

CONCLUSION

Lateral pancreaticojejunostomy results in significant improvement in quality of life, resolution of abdominal pain, and reduction in opioid consumption in patients with chronic pancreatitis.

LIMITATIONS & RECOMMENDATIONS

Our study has several limitations. The follow-up period was short. Future studies with longer follow-up duration are suggested. Moreover, randomized

controlled trials are recommended for comparing it with other surgical modalities.

Conflict of Interest: None.

Source of Funding: None.

Authors' Contributions:

N.B: Study design and methodology, manuscript drafting and approval Literature review and referencing and manuscript review

M.T: Paper writing, critical review, and manuscript approval

A.S: Data collection, analysis and manuscript approval

A.A.T: Analysis of data and interpretation of results, Editing and quality insurance, drafting and manuscript approval

REFERENCES

1. Cai QY, Tan K, Zhang XL, Han X, Pan JP, Huang ZY, et al. Incidence, prevalence, and comorbidities of chronic pancreatitis: a 7-year population-based study. World J Gastroenterol. 2023; 29(30):4671-84. doi:10.3748/wjg.v29.i30.4671.

2. Singh VK, Yadav D, Garg PK. Diagnosis and management of chronic pancreatitis: a review. JAMA. 2019; 322(24):2422-34. doi:10.1001/jama.2019.19411.

3. Hart PA, Conwell DL. Chronic pancreatitis: managing a difficult disease. Am J Gastroenterol. 2020; 115(1):49-55. doi:10.14309/ajg.0000000000000421.

4. de Rijk FEM, van Veldhuisen CL, Kempeneers MA, Issa Y, Boermeester MA, Besselink MG, et al. Quality of life in patients with definite chronic pancreatitis: a nationwide longitudinal cohort study. Am J Gastroenterol. 2023; 118(8):1428-38. doi:10.14309/ajg.0000000000002266.

5. Ramsey ML, Conwell DL, Hart PA. Chronic pancreatitis. Yamada's Textbook of Gastroenterology. 2022:1602-15. doi:10.1002/9781119600206.ch76.

6. Szatmary P, Grammatikopoulos T, Cai W, Huang W, Mukherjee R, Halloran C, et al. Acute pancreatitis: diagnosis and treatment. Drugs. 2022; 82(12):1251-76. doi:10.1007/s40265-022-01766-4.

7. Kempeneers MA, Issa Y, Ali UA, Baron RD, Besselink MG, Buchler M, et al. International consensus guidelines for surgery and the timing of intervention in chronic pancreatitis. Pancreatology. 2020; 20(2):149-57. doi:10.1016/j.pan.2019.12.005.

8. Nathan JD, Ellery K, Balakrishnan K, Bhatt H, Ganoza A, Husain SZ, et al. The role of surgical management in chronic pancreatitis in children: a position paper from the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition Pancreas Committee. J Pediatr Gastroenterol Nutr. 2022; 74(5):706-19. doi:10.1097/MPG.0000000000003439.

9. Gujar AA, Gujar AA, Dharia A. Open modified puestow procedure in an advanced endoscopic era for chronic pancreatitis with dilated pancreatic duct and stones. Int J Surg. 2020; 4(3):71-6. doi:10.33545/surgery.2020.v4.i3b.471.

10. Maharaj R, Haralsingh A, Mohammed J, Ramnarace K, Lee-Cazabon H. Modified puestow procedure for chronic pancreatitis in an adolescent female. Cureus. 2022; 14(5):e25503. doi:10.7759/cureus.25503.

11. World Health Organization. WHOQOL: Measuring Quality of Life. Available from: https://www.who.int/tools/whoqol/whoqol-bref.

12. Child Outcomes Research Consortium. Paediatric Quality of Life (PedsQL). Available from: https://www.corc.uk.net/outcome-experience-measures/paediatric-quality-of-life-pedsql.

13. Sah DN, Bhandari RS, Singh YP, Vaidya P, Kansakar PBS, Ghimire B, et al. Early outcome of Frey's procedure for chronic pancreatitis: Nepalese tertiary center experience. BMC Surg. 2019; 19(1):139. doi:10.1186/s12893-019-0592-7.

14. Rege S, Banker A, Shah S, Bhesania D. Long-term outcomes of laparoscopic longitudinal pancreatojejunostomy and modified Frey's procedure for patients of chronic pancreatitis: a 10-year experience. J Minim Access Surg. 2024; 20(1):74-80. doi:10.4103/jmas.jmas_282_22.

15. Islam SR, Rahman S, Talukdar S, Sarkar SA, Poran S, Rahman M. Lateral pancreato-jejunostomy in chronic pancreatitis: an appraisal of 32 cases. Arch Surg Clin Res. 2020; 4:001-5. doi:10.29328/journal.ascr.1001043.

16. Baste NM, Patil V, Radhakrishna S. Clinical outcomes of lateral pancreaticojejunostomy for chronic calcific pancreatitis - an observational study. Neuroquantology. 2022; 20(19):3918-21. doi:10.48047/NQ.2022.20.19.NQ99353.

17. Hodgman E, Megison S, Murphy JT. Puestow procedure for the management of pediatric chronic pancreatitis. Eur J Pediatr Surg. 2019; 29(2):153-8. doi:10.1055/s-0037-1608938.

18. Yang CJ, Bliss LA, Freedman SD, Sheth S, Vollmer CM, Ng SC, et al. Surgery for chronic pancreatitis: the role of early surgery in pain management. Pancreas. 2015; 44(5):819-23. doi:10.1097/MPA.0000000000000333.

19. Pakosz-Golanowska M, Post M, Lubikowski J, Butkiewicz J, Białek A, Raszeja-Wyszomirska J, et al. Partington-Rochelle pancreaticojejunostomy for chronic pancreatitis: analysis of outcome including quality of life. Hepatogastroenterology. 2009; 56(94-95):1533-7. Available from: https://pubmed.ncbi.nlm.nih.gov/19950824l.

20. Waage A, Vinge-Holmquist O, Labori KJ, Paulsen V, Aabakken L, Lenz H, et al. Tailored surgery in chronic pancreatitis after implementation of a multidisciplinary team assessment; a prospective observational study. HPB (Oxford). 2022; 24(12):2157-66. doi:10.1016/j.hpb.2022.09.007.

21. Kalady MF, Broome AH, Meyers WC, Pappas TN. Immediate and long-term outcomes after lateral pancreaticojejunostomy for chronic pancreatitis. Am Surg. 2001; 67(5):478-83. doi:10.1177/00031348010670052.

22. Manapure SB, Munde AS, Kasale RJ, Lokare P. A clinical study on lateral pancreaticojejunostomy in a case of chronic pancreatitis. Int Sur J. 2021; 8(5):1617-20. doi:10.18203/2349-2902.isj20211842.

23. Varshney VK, Nayar R, Hussain S, Selvakumar B. Total robotic lateral pancreaticojejunostomy and modified Frey's procedure for chronic calcific pancreatitis. Langenbecks Arch Surg. 2022; 408(1):1. doi:10.1007/s00423-022-02735-x.

24. Kempeneers MA, van Hemert AKE, van der Hoek M, Issa Y, van Hooft JE, Nio CY, et al. Short- and long-term outcomes of selective use of Frey or extended lateral pancreaticojejunostomy in chronic pancreatitis. Br J Surg. 2022; 109(4):363-71. doi:10.1093/bjs/znab473.

25. Bhandarwar A, Arora E, Gajbhiye R, Gandhi S, Patel C, Wagh A, et al. Laparoscopic lateral pancreaticojejunostomy: an evolution to endostapled technique. Surg Endosc. 2019; 33(6):1749-56. doi:10.1007/s00464-018-6434-3.

26. Nag HH, Arvinda PS, Sachan A, Saluja SS, Sachdeva S, Chandra S. Laparoscopic lateral pancreaticojejunostomy - the technique and early experience. Indian J Surg. 2019; 81(1):51-6. doi:10.1007/s12262-018-1734-3.

Original Article

Ipsative Assessment in Medical Education: Enhancing Self-Reflection and Competency Development

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ABSTRACT

Objective: To investigate the efficacy of ipsative assessment in medical education.

Methodology: A phenomenological qualitative research methodology was used to conduct one-on-one semi-structured interviews with medical students during various training phases at Sahara Medical College, Narowal from May to July 2023. A total of 20 medical students from a private college participated in the study. The Otter web program was used to do a thematic analysis of the qualitative data acquired during interviews.

Results: Ipsative assessment enhanced self-awareness and self-regulation in medical students, encouraging a culture of continual progress. Participants noted increased personal development and a focus on individual learning objectives. Ipsative assessment was viewed as an effective approach for competency improvement.

Conclusion: Ipsative assessment has incredible potential in medical education, putting students at the core of their educational experience. It promotes self-directed learning, self-awareness, and continuous growth for medical students.

Keywords: *Self-regulation. Ipsative assessment. Medical education.*

INTRODUCTION

Ipsative assessment is an assessment emphasizing students' progress by comparing them to how they were performing before rather than how others around them are functioning or a set standard. This is primarily defined by personal improvement and is established on a system of continuous development, encouraging the learner to reflect on their inferior and superior capabilities.[1] In ipsative assessment, students are assessed against their own baseline, embedding self-reflective learning, self-regulation, and self-direction.[2,3] Such an approach confirms current educational theorists and practices, especially in educational environments where personalized learning and competency-based education are key priorities. Ipsative assessment aims to make students think about their educational experiences and empower them to develop a culture of ongoing improvement, personal, and professional growth. This type of self-assessment empowers the students to achieve their goals.[4]

Medical education is a continuously evolving field that tends to meet the needs of the growing healthcare system.[5] The primary issue of concern is the assessment of medical students' competency and readiness for clinical practice. Historically, medical education has utilized norm-referenced exams for evaluation. Nonetheless, they theoretically overlook each learner's individual areas of development to categorize learners in relation to classmates.[6] However, recent progress in educational theory and practice has introduced a change in assessment paradigms in medical education. Ipsative assessment is a growing paradigm focusing on an individual's growth and development in terms of his/her previous performance.[7] This reflects a wider educational move towards valuing personal development, growth in experience, and independent learning. Ipsative assessment is a promising method for enabling medical learners to assess their competence and development of self-reflection.[5]

If incorporated into an existing system, example being the standards of the Accreditation Council for Graduate Medical Education in the United States and similar accreditation bodies around the world, ipsative assessment can help drive system transformation. Modern theories of adult learning, such as self-directed learning (SDL), have also argued that students need to be active participants in their education. This further emphasizes the importance of self-regulation, reflection, and evolution in the cultivation of fluency, as well as adaptability, in our healthcare workforce.[8]

The purpose of this study was to explore how ipsative assessment improves the medical student's self-reflection and competency growth and what are the issues that may be faced.

METHODOLOGY

This phenomenological qualitative study was conducted in interpretivist paradigm. After approval from ethical review board of the institution (Letter No: ERC/0030/2023, 10-01-2023), this study was conducted at Sahara Medical College, Narowal from May to July 2023. A total of 20 participants were taken from all 5 years of MBBS (4 from each). Data was collected through semi-structured interviews with

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open-ended questions, according to the interview guide to explore an in-depth perspective of ipsative assessment. Informed written consent was obtained from all participants before the interviews. They were informed about the study's purpose, voluntary participation, and the confidentiality of their responses. Depending on the preferences of the participants, the interviews were performed in person or by video conference in a quiet and comfortable environment. Usually lasting between thirty and sixty minutes, each interview allowed for in-depth conversations. Essential observations, thoughts, and ideas about the interview were recorded at the same time, to be used in data analysis. Participants were informed about the interview before time. Interviews were conducted in areas free from distraction and suitable for the participants. The interviews were audio-recorded to ensure accuracy in capturing their responses.

Confidentiality was maintained by ensuring that all participants' identities and responses were anonymized. Each participant was assigned a unique identifier to replace their personal information, such as their name or contact details, in the transcripts and any other documentation. Additionally, access to the data was restricted to the research team only, and measures were put in place to securely store and transmit the data, such as encryption and password protection.

DATA ANALYSIS

The audio recordings of the interviews were transcribed into written text using the Otter online application. The transcripts were systematically analyzed line by line. Codes or labels were assigned to segments of text representing specific concepts, themes, or patterns related to ipsative assessment. Codes were then organized into broader themes or categories, representing the key findings or recurring patterns in the qualitative data. The researchers interpreted the themes, exploring their meaning and significance in the context of the research questions. This involves a qualitative understanding of the data rather than statistical analysis.

The interpretivist paradigm was used, recognizing that participants' experiences are influenced by their individual interpretations and contexts.[9] Data was collected and analyzed continually until redundancy was reached in order to achieve data saturation in our study. To develop a deeper, more comprehensive understanding of students' perspectives, the researcher used a variety of data sources, primarily semi-structured interviews with participants, observations, and field notes taken by the researcher during the interview. A number of steps were taken to ensure validity. We used member checking in conjunction with a participatory approach to establish interpretative validity. The participants reviewed the transcripts in order to verify the precision of the interviews. The excerpts provided in each of the themes further proved the descriptive validity. The study topic (research question), transcripts, and matrices were reviewed on a regular basis by a group of researchers (member checking), who tested each other's interpretations for plausibility, robustness, and conformability before coming to a final conclusion.

RESULTS

A total of 20 students responded to the survey. Fostering self-awareness, enhancing self-regulation, personal growth, learning goals, self-reflection, continuous improvement, and competency development are the various themes emerged from the students. Major themes, subthemes, and students' responses are shown in Table 1. Figure 1 shows word cloud showing the impact of self-reflection and competency development highlighted by the students.

Figure 1: Word Cloud showing the Impact of Self-Reflection and Competency Development Highlighted by the Students

Table 2: Formation of Themes and Subthemes along with Relevant Verbatim

Themes	Subthemes	Verbatim Quotes
Fostering Self-Awareness	**Identifying Strengths and Weaknesses**	"With new understanding of this form of assessment, *I found that ipsative assessment really made me think about where I stand compared to where I want to be."*
		"When I see myself in the mirror relating to this new assessment tool, knowing that I'm being assessed based on my own progress, pushes me to stay on track and regulate my own learning."
	Objective Self-Appraisal	*"With ipsative assessment, I can see where I need to improve without feeling like I'm being compared to others."*
	Motivation for Self-Improvement	*"The awareness of areas needing improvement can serve as a powerful motivator, pushing students to invest time and effort in enhancing their competencies."*
Enhancing Self-Regulation	**Goal Setting**	*"As undergraduate medical student, I think the goal setting is an important tool to progress on daily basis. Setting clear goals with ipsative assessment helps me stay focused and motivated."*
	Monitoring Progress	*"Linking my 4th year log book, regularly checking my progress against my goals helps me stay on track and adjust my study strategies as needed."*
	Adaptive Learning Strategies	*"We have been familiarized with new learning strategies during our PERL module by the medical educationist so, if I notice I'm struggling with a topic, ipsative assessment prompts me to try different study methods until I find what works best for me."*
	Ownership of Learning	*"When I was in my junior years I was not able to take ownership and I used to blame others for failing in any exam. Now in final year with knowledge of ipsative, I feel more responsible for my own learning. It's up to me to make the most of my education."*
Personal Growth	**Heightened Sense of Personal Growth**	*"I feel like I've grown so much as a learner since I started focusing on my own development rather than comparing myself to others."*
		"I never realized how much I could improve until I started using ipsative assessment. It's like a journey of self-discovery."
Learning Goals	**Individualized Learning Objectives**	*"Mostly the main aim and objective of a medical student, genuinely, is to pass the exam and how to do that is a million-dollar question. This new knowledge of ipsative assessment encourages me to set goals that are meaningful to me and my future as a medical professional."*
		"Instead of just trying to meet the standard, ipsative assessment encourages me to set my own standards and strive for excellence."
Self-Reflection	**Facilitating Meaningful Self-Reflection**	*"Reflection is the best tool to progress and to improve anything in your life. The feedback I get from ipsative assessment helps me reflect on my strengths and weaknesses, which in turn helps me improve."*
		"I never used to reflect on my learning much, but now with my friends and peers, ipsative assessment has really changed that by observing them and making things change, I'm constantly thinking about what I can do better."
Continuous Improvement	**Promoting a Culture of Continuous Improvement**	*"Initially my aim was to pass the exam and to get through. Now with strong guidance of my teachers, I am thinking out of the box to set a broader vision, and with ipsative assessment, I see every challenge as an opportunity to grow."*
		"The teacher mentioned in the session that nothing can be stolen from us, ipsative assessment makes us want to improve ourselves for the better "Nobody can steal things from you."
Competency Development	**Perceived Value for Competency Development**	*"From the perspective of the ipsative assessment, I think it is a beneficial element to help improve the areas of behavior I want to focus on in my future perspectives"*
		"The fact that ipsative assessment is centered on my competencies as opposed to my scores within examinations, makes it more purposeful in my endeavor to become a doctor".

DISCUSSION

Qualitative analysis on ipsative assessment in medical education has provided considerable findings in enhancing self-awareness, regulating self-development of personality, and focusing on personal learning objectives of medical students. It also highlights, how the task value of ipsative assessment as a tool for competency development has been framed.[9]

Ipsative assessment increases the self-awareness and self-regulation skills in students, which is identified in our study. This is in line with the principles of SDL that adult education theory advocates.[8] van der Vleuten et al. also suggests that learning is a social process but as learning becomes more embedded in the individual, it moves from an external regulatory type of control to an internal type of self-regulation.[2] Ipsative assessment meets this transition by engaging students to be more involved in their learning practice. This observation confirms the results of a new study undertaken by Ilhan. This highlights the significance of self-regulation for academic success.[10] Recent reviews by Chen et al. highlight the necessity for self-regulation and reflective practice in health professions education.[11] By presenting our results in the light of these new publications, we re-emphasize the importance of ipsative assessment in current medical education contexts.[12]

In the present study, ipsative assessment also had a positive influence on medical students' self-awareness. This means students began to be more aware of their own qualities and shortfalls; especially with respect to their work as well as what they need to work on. The results of our study support those of previous research, indicating the need to adapt teaching practices to the premises of self-directed learning, as this is likely to increase students' understanding of their learning process and promote self-regulation.[13]

This idea is echoed in the numerous accounts of the participants in the study elaborating that they experience a personal development upon getting engaged in some of the activities contained in the ipsative assessment.[14] Ipsative assessment also enables the student to make independent evaluations of performance, thus making it to be transformative in learning. Additionally, the shift to specific learning outcomes in line with the concept of ipsative Assessment also led to capacitation in improving the compliance to diverse goals of the medical students. In the recent past, a study pointed to the lack of competency models in medical education because students are highly diverse and have different competencies and learning needs. Thus, they require different learning environment.[11]

The findings of our study thus reveal that the mechanism of ipsative assessment enhances Medical Education toward future improvement. This is well explained under the framework of lifelong learning which is gaining recognition of importance, especially in medical education.[10] Thus, in conjunction with self-reflection and the emphasis placed on students' purposeful goal-setting for their learning process, ipsative assessment contributes to the formation of a 'growth mindset.

This view has been enhanced through students' impression about competency-based medical education (CBME) by covet and ipsative assessment as a competent tool for fostering their competencies.[15] Competency-based medical education as a development approach, focuses more on attaining specific competencies/objectives rather than time-based progression. Ipsative assessment is a feasible development for the implementation of CBME since it helps provide better feedback on core competencies and personal traits and provides options for individualized development.[15] The value of ipsative assessment was revealed from the students' perspective as an important tool in competency formation that aligns with CBME principles.[12] This is in agreement with another study by Sandars, in which the elements of reciprocal peer teaching and peer feedback are found to be beneficial in developing students' clinical competence.[7]

The research findings of our study correspond to recent publications that are relevant to medical education and assessment. A recent study has highlighted personalization and deliberate practice as two essential strategies for promoting self-regulation in health education, arts, and social sciences. These incorporate the value of reflection as a means of enhancing knowledge acquisition and enhancing the practice of the health care profession.[9]

CONCLUSION

Self-assessment opens the door as a useful technique in the modern medical training setting. Ipsative assessment has the power to reshape students' learning path because it places students, not teachers, at the heart of the whole educational process. Our research has shown that ipsative assessment is a feasible tool for the advancement of self-actualization and learning.

LIMITATIONS & RECOMMENDATIONS

The study was done in a single private medical college and thus had some limitations in its generalization. To have a wider standpoint and to cover contextual factors, further research needs to be conducted with the participation of different medical colleges and universities. The study did not include quantitative data measurement and analysis. It is therefore imperative to incorporate numeric data, for example, surveys, administered tests, etc. to supplement this study in view to assess the effect of ipsative assessment on learning and performance.

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Authors' Contributions:
F.S: Concept Design, initial Write-up, Final approval of the version to be published
A.Z: Critically analysis of research methodology and final draft
S.N.M: Data Collection and Analysis
G.A: Data Collection and Analysis
M.A.B.A: Data Collection and Analysis
S.L: Data Collection and Analysis
F.I: Data Collection
H.K: Data Collection

REFERENCES

1. Seery N, Buckley J, Delahunty T, Canty D. Integrating learners into the assessment process using adaptive comparative judgement with an ipsative approach to identifying competence based gains relative to student ability levels. Int J Technol Des Educ. 2019; 29:701-15. doi:10.1007/s10798-018-9468-x.

2. van der Vleuten CPM, Schuwirth LWT. Assessment in the context of problem-based learning. Adv Health Sci Educ Theory Pract. 2019; 24(5):903-14. doi:10.1007/s10459-019-09909-1.

3. Burke D. Assessment and appraisal. How Doctors Think and Learn. Springer, Cham. 2020:65-74 doi:10.1007/978-3-030-46279-6_9.

4. Saiyad S, Bhagat P, Virk A, Mahajan R, Singh T. Changing assessment scenarios: lessons for changing practice. Int J Appl Basic Med Res. 2021; 11(4):206-13. doi:10.4103/ijabmr.IJABMR_334_21.

5. Watling CJ, Ginsburg S. Assessment, feedback and the alchemy of learning. Med Educ. 2019; 53(1):76-85. doi:10.1111/medu.13645.

6. Wetzel E, Frick S, Greiff S. The multidimensional forced-choice format as an alternative for rating scales - current state of the research. EJPA. 2020; 36(4):511-5. doi:10.1027/1015-5759/a000609.

7. Sandars J. Self-regulated learning: the essential factor for understanding and improving academic and clinical performance. ScientiaMedica. 2020; 30(1):e36232. doi:10.15448/1980-6108.2020.1.36232.

8. Dahal A, BhatN. Self-directed learning, its implementation, and challenges: a review. Nepal J Health Sci. 2023; 3(1):102-15. doi:10.3126/njhs.v3i1.63277.

9. Anazor F. Ipsative assessment and peer feedback in an orthopaedic junior doctor teaching programme: a project plan and narrative review of the literature. Cureus. 2022; 14(11):e31961. doi:10.7759/cureus.31961.

10. Ilhan E. Evaluation of competency based medical education curriculum. IJPE. 2021; 17(3):153-68. doi:10.29329/ijpe.2021.346.10.

11. Chen CW, Wang WC, Mok MMC, Scherer R. A lognormal ipsative model for multidimensional compositional items. Front Psychol. 2021; 12:573252. doi:10.3389/fpsyg.2021.573252.

12. Stanislaw H, McCreary J. Identifying Core values with a hierarchical, ipsative, preference assessment. J Pers Assess. 2023; 105(3):329-41. doi:10.1080/00223891.2022.2090369.

13. Martinez A, Salgado JF. A meta-analysis of the faking resistance of forced-choice personality inventories. Front Psychol. 2021; 12:732241. doi:10.3389/fpsyg.2021.732241.

14. Malecka B, Ajjawi R, Boud D, Tai J. An empirical study of student action from ipsative design of feedback processes. Assess. Eval. High. Educ. 2021; 47(5):801-15. doi:10.1080/02602938.2021.1968338.

15. Penrabel RP, de Oliveira Bastos PR, Biberg-Salum TG. The perspectives and challenges of the competency-based curriculum in medical education: a literature review. Creat Educ. 2022; 13(10):3191-203. doi:10.4236/ce.2022.1310203.

Original Article

Pulmonary Hypertension in Patients with Connective Tissue Disorders and Impaired Six Minute Walk Test

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ABSTRACT

Objective: To determine the frequency of pulmonary hypertension in patients with connective tissue disorders with impaired six-minute walk test.

Methodology: This descriptive cross-sectional study was conducted at the Department of Cardiology, Shaikh Zayed Hospital and Sharif Medical City Hospital, Lahore from October 2023 to March 2024. A total of 63 patients from both genders, aged between 20-50 years diagnosed with connective tissue disorder for at least 1 year having impaired 6-minute walk test were included. Informed written consent was taken from the patients. Non-probability convenient sampling technique was used to enroll patients. These patients underwent echocardiography and pulmonary hypertension was diagnosed if mean pulmonary artery pressure (mPAP) was >25 mmHg. Frequency of pulmonary hypertension was noted and data was stratified for age, gender, body mass index (BMI), residential status, and duration of disease. The Statistical Package for the Social Sciences (SPSS) version 24.0 was used for data analysis.

Results: The mean age of patients was 36.7±7.7 years with 9(14.3%) males and 54(85.7%) females. The mean BMI of the patients was 26.8±3.8 kg/m^2 while the mean duration of the disease was 3.7±1.4 years. The majority of the patients [37(58.7%)] were rural residents. Pulmonary hypertension was diagnosed in 7(11.1%) patients with connective tissue disorders and impaired 6-minute walk test. When stratified, the difference was insignificant across various subgroups of age (p=0.789), gender (p=1.000), BMI (p=0.754), residential status (p=0.928), and duration of disease (p=0.923).

Conclusion: A substantial proportion of patients with connective tissue disorders and impaired 6-minute walk test had undiagnosed pulmonary hypertension irrespective of age, gender, BMI, residential status, and duration of disease of patients.

Keywords: *Pulmonary hypertension.* Connective Tissue Disorders

INTRODUCTION

Pulmonary hypertension (PH), characterized by elevated blood pressure in the pulmonary arteries, stems from various causes, including connective tissue disorders (CTDs).[1] This complex cardiovascular condition often leads to complications such as right heart failure, exertional dyspnea, and impaired exercise tolerance. Pulmonary hypertension is now recognized as a prevalent and severe complication arising from connective tissue diseases. While PH typically manifests later in the course of these diseases, regular visits to rheumatologists or internists create a unique opportunity for early screening. This proactive approach facilitates timely intervention, potentially curbing the progression of pulmonary hypertension and averting premature mortality.[2]

Connective tissue disorders encompass a spectrum of autoimmune and inflammatory conditions affecting the structural framework of the body. Among them, systemic sclerosis, systemic lupus erythematosus, and rheumatoid arthritis have been notably linked to an increased risk of developing pulmonary hypertension.[3] The intricate mechanisms underlying this association involve chronic inflammation, vascular remodeling, and fibrosis, collectively contributing to pulmonary vascular resistance and ultimately, PH.[4]

Compounding the complexity of this relationship, impaired exercise capacity, as assessed by the six-minute walk test (6MWT), emerges as a crucial indicator of disease severity.[3] The 6MWT gauges functional capacity and reflects the ability of individuals to perform daily activities. In the context of PH and CTDs, a compromised 6MWT underscores the impact of pulmonary vascular involvement on physical well-being.[5]

Existing literature has controversial results regarding the frequency of pulmonary hypertension in cases with connective tissue disorders and impaired six-minute walk test ranging from 11.4% reported in Pakistan to 20.51% in Korea.[6]

Given the variations in reported frequencies, this study was undertaken to ascertain this association between connective tissue disorders with impaired 6MWT, and pulmonary hypertension. By producing existing literature and addressing gaps in knowledge, this research aims to contribute valuable insights that

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may inform clinical management strategies and improve the overall care of individuals grappling with the complex interplay of PH and CTDs, in future practice.

METHODOLOGY

This descriptive cross-sectional study was conducted at the Department of Cardiology, Shaikh Zayed Hospital and Sharif Medical City Hospital, Lahore from October 2023 to March 2024. After approval from the ethical review committee (Letter No. SMDC/SMRC/309-23, 19-09-2023), 63 patients were included with a 95% confidence level and 10% margin of error with the anticipated frequency of pulmonary hypertension in cases with CTD and impaired six-minute walk test as 20.51% in previous studies.[7] Non-probability convenient sampling technique was used to enroll patients. An informed consent was taken from all the subjects and baseline characteristics were noted. Inclusion criteria were patients of both genders with age between 20-50 years and diagnosed with connective tissue disorders that were documented cases of rheumatoid arthritis, systemic lupus erythematosus, scleroderma, Sjogern syndrome for at least 1 year. The exclusion criterion was patients with valvular heart diseases, congenital heart diseases, limitation in walking, heart failure, or end-stage renal or liver failure. Then all of these cases underwent a minute walk test. The patients were asked to walk on the hard flat hall of at least length of 30 m for six minutes. The patient increased the pace slowly on instructions. Pulse oximeter was used to monitor the oxygen saturation level. The patients were monitored by a resident doctor. Impaired 6MWT was labelled where the distance covered in 6 minutes was less than 0.26 miles or oxygen checked on the pulse oximeter dropped below 90%. Pulmonary Hypertension was assessed on the basis of echocardiography and was labelled as yes where mPAP was >25 mmHg.[8] The patients with impaired 6MWT underwent transthoracic echocardiography by a consultant with at least 1 year post-fellowship experience. Data regarding age, gender, BMI, residential status, and duration of disease. All of these results were collected and recorded on the proforma.

STATISTICAL ANALYSIS

The Statistical Package for the Social Sciences (SPSS) version 24.0 was used for data analysis. For quantitative variables such as age, BMI, and duration of connective tissue disorder, mean±SD was calculated. Frequencies and percentages were used for categorical variables i.e. gender, residential status, and presence of pulmonary hypertension. To address effect modifiers, the frequency of pulmonary hypertension was stratified for age, gender, BMI, residence, and duration of connective tissue disorder, and Chi-square test was applied. A p-value of ≤0.05 was taken as significant.

RESULTS

The age distribution of the study participants varied from 20-50 years with a mean age of 36.7±7.7 years. A significant proportion 33(52.4%) of the subjects were 35 years old or older. Gender distribution revealed 9(14.3%) male and 54(85.7%) female patients. The mean BMI was 26.8±3.8 kg/m^2. Obesity was observed in 15(23.8%) participants. The majority of the participants [37(58.7%)] resided in rural areas. The mean duration of disease was 3.7±1.4 years as shown in Table 1. Pulmonary hypertension was diagnosed in 7(11.1%) patients with connective tissue disorder and impaired 6-minute walk test. When stratified, the difference was insignificant for age (p=0.789), gender (p=1.000), BMI (p-value=0.754), residential status (p=0.928), and duration of disease (p=0.923) as given in Table 2.

Table 1: Demographic Features of Study Participants

Study Variables		Descriptive Statistics
Age (Years)	**Mean±SD**	36.7±7.7
	<35	30(47.6%)
	≥35	33(52.4%)
Gender	**Male**	9(14.3%)
	Female	54(85.7%)
BMI (kg/m^2)	**Non-Obese (<30)**	48(76.2%)
	Obese (≥30)	15(23.8%)
Residence	**Rural**	37(58.7%)
	Urban	26(41.3%)
Duration of Disease (Years)	**Mean±SD**	3.7±1.4
	<4 years	19(30.2%)
	≥4 years	44(69.8%)

Table 2: Stratification of PH according to Age, Gender, BMI, Residency, and Duration of Disease

Study Variables		Pulmonary Hypertension Frequency & Percentage		p-value
		Yes	No	
Age (Years)	**<35**	3(10.0%)	27(90.0%)	0.789
	≥35	4(12.1%)	29(87.9%)	
Gender	**Male**	1(11.1%)	8(88.9%)	1.000
	Female	6(11.1%)	48(88.9%)	
BMI (kg/m^2)	**Non-Obese (<30)**	5(10.4%)	43(89.6%)	0.754
	Obese (≥30)	2(13.3%)	13(86.7%)	
Residence	**Rural**	4(10.8%)	33(89.2%)	0.928
	Urban	3(11.5%)	23(88.5%)	
Duration of Disease (Years)	**<4**	2(10.5%)	17(89.5%)	0.923
	≥4	5(11.4%)	39(88.6%)	

DISCUSSION

Pulmonary hypertension is a progressive condition characterized by heightened pulmonary arterial pressure and increased vascular resistance, leading to the potential development of right heart failure and increased mortality risk.[9] Despite being categorized as an orphan disease, its prevalence, encompassing all subtypes, can extend up to 15 cases per million.[10] Unfortunately, conventional symptoms and physical examinations prove inadequate for early PH detection, primarily due to their delayed onset and non-specific nature. Hence, emphasizing early detection strategies during routine medical consultations becomes pivotal in mitigating its impact.[11,12] Echocardiography is a useful tool in the diagnosis but it cannot be performed in routine unless there is a high index of suspicion.[5]

In this study, patients diagnosed with connective tissue diseases exhibited a mean age of 36.7±7.7 years. The gender distribution revealed 9 (14.3%) male and 54 (85.7%) female patients, resulting in a male-to-female ratio of 1:6. Mean duration of the disease was 3.7±1.4 years.

Ahsan et al. studied 603 patients presenting with connective tissue disease at Jinnah Postgraduate Medical Centre, Karachi and reported a mean age of 35.2±12 years.[13] They observed a similar female predominance among such patients with a male-to-female ratio of 1:4. Mean duration of disease in their series was 3.2±2 years. In another recent study conducted by Dahani et al. at the same institute, the authors reported a similar mean age of 35.1±12.5 years among such patients and a male-to-female ratio of 1:9. Mean duration of disease in their series was 3.8±4.3 years.[14] Another Indian study observed a comparable mean age of 38.2±14.5 years among such patients. They reported comparable female predominance with male to female ratio of 1:2.1.[15]

In the present study, pulmonary hypertension was diagnosed in 7 (11.1%) patients with connective tissue disorders and impaired 6-minute walk test. When stratified, no statistically significant difference was observed in the frequency of pulmonary hypertension across various subgroups of patients based on age (p-value=0.789), gender (p-value=1.000), BMI (p-value=0.754), residential status (p-value=0.928) and duration of disease (p-value=0.923).

Another study reported that 11.4% of patients with connective tissue diseases had previously undiagnosed pulmonary hypertension.[14] Similar frequency of pulmonary hypertension (11.6%) was noted among patients with CTDs in another study.[16] These findings align with the study by Jung et al. in Korea, who reported a prevalence of 10.7%.[17] The varying prevalence rates across different regions and studies highlight the importance of continued vigilance and comprehensive screening strategies for early detection and management of pulmonary hypertension in this patient population. Such insights contribute to a deeper understanding of the disease burden and aid in the development of targeted interventions to improve patient outcomes and quality of life.[17] Another study found an insignificant difference for subgroups of age (p=0.789), gender (p=1.000), BMI (p-value=0.754), residential status (p=0.928) and duration of disease (p=0.923).[15]

CONCLUSION

A substantial proportion of patients with connective tissue disorders and impaired 6-minute walk test had undiagnosed pulmonary hypertension irrespective of age, gender, BMI, residential status, and duration of disease of patients. This advocates routine echocardiographic screening of such patients for

timely diagnosis and management of pulmonary hypertension.

LIMITATIONS & RECOMMENDATIONS

A significant limitation of this study was the lack of association between the presence of pulmonary hypertension, its outcome, and the specific type of underlying connective tissue disease. Further studies were recommended to address this gap, and such a study is strongly recommended.

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Authors' Contributions:

S.M: Conceived study data, prepared synopsis, and collected data

U.F: Conceived study data, prepared synopsis, and collected data

M.A.K: Supervised work, data analysis, and write-up of research paper

A.A: Supervised work, data analysis, and write-up of research paper

N.G: Supervised work, data analysis, and write-up of research paper

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REFERENCES

1. Vonk MC, Vandecasteele E, van Dijk AP. Pulmonary hypertension in connective tissue diseases, new evidence and challenges. Eur J Clin Invest. 2021; 51(4):e13453. doi:10.1111/eci.13453.
2. Khangoora V, Bernstein EJ, King CS, Shlobin OA. Connective tissue disease-associated pulmonary hypertension: a comprehensive review. Pulm Circ. 2023; 13(4):e12276. doi:10.1002/pul2.12276.
3. Costa GOS, Ramos RP, Oliveira RKF, Cepeda A, Vieira EB, Ivanaga IT, et al. Prognostic value of six-minute walk distance at a South American pulmonary hypertension referral center. Pulm Circ. 2020; 10(2):2045894019888422. doi:10.1177/2045894019888422.
4. Yoshitomi Y, Suwa Y, Tsuchiya H, Goto M, Natsumoto B, Shoda H, et al. Pulmonary hypertension associated with anti-synthetase syndrome: a case report and literature review. Intern Med. 2023; 62(24):3685-9. doi:10.2169/internalmedicine.9809-22.
5. Almaaitah S, Highland KB, Tonelli AR. Management of pulmonary arterial hypertension in patients with systemic sclerosis. Integr Blood Press Control. 2020; 13:15-29. doi:10.2147/IBPC.S232038.
6. Kusunose K, Yamada H, Hotchi J, Bando M, Nishio S, Hirata Y, et al. Prediction of future overt pulmonary hypertension by 6-min walk stress echocardiography in patients with connective tissue disease. J Am Coll Cardiol. 2015; 66(4):376-84. doi:10.1016/j.jacc.2015.05.032.
7. Waxman AB, Elia D, Adir Y, Humbert M, Harari S. Recent advances in the management of pulmonary hypertension with interstitial lung disease. Eur Respir Rev. 2022; 31(165):210220. doi:10.1183/16000617.0220-2021.
8. Choi JH, Shin MJ, Lee BJ, Park JH. Exercise-induced desaturation during a six-minute walk test is associated with poor clinical outcomes in patients with pulmonary arterial hypertension. Clin Hypertens. 2023; 29(1):33. doi:10.1186/s40885-023-00256-3.
9. Rezende CF, Mancuzo EV, Correa RA. Heart rate recovery in 1 minute after the 6-minute walk test predicts adverse outcomes in pulmonary arterial hypertension. PLoS One. 2022; 17(5):e0268839. doi:10.1371/journal.pone.0268839.
10. Smukowska-Gorynia A, Gosciniak W, Wozniak P, Iwanczyk S, Jaxa-Kwiatkowska K, Slawek-Szmyt S, et al. Recent advances in the treatment of pulmonary arterial hypertension associated with connective tissue diseases. Pharmaceuticals (Basel). 2023; 16(9):1252. doi:10.3390/ph16091252.
11. Dong C, Li Y. Exercise rehabilitation training in patients with pulmonary hypertension: a review. Heart Lung Circ. 2022; 31(10):1341-8. doi:10.1016/j.hlc.2022.06.660.
12. Rahaghi FF, Kolaitis NA, Adegunsoye A, de Andrade JA, Flaherty KR, Lancaster LH, et al. Screening strategies for pulmonary hypertension in patients with interstitial lung disease: a multidisciplinary Delphi study. Chest. 2022; 162(1):145-55. doi:10.1016/j.chest.2022.02.012.
13. Ahsan T, Erum U, Dahani A, Khowaja D. Clinical and immunological profile in patients with mixed connective tissue disease. J Pak Med Assoc. 2018; 68(6):959-62. Available from: https://www.archive.jpma.org.pk/PdfDownload/8742.
14. Dahani A, Arain SR, Riaz A, Khan F, Jabeen R. Prevalence and pattern of pulmonary manifestation in patients with connective tissue disorder. Cureus. 2020; 12(4):e7618. doi:10.7759/cureus.7618.
15. Kadiru RA, Hegde SP, Shenoy MM. An observational cross-sectional study of varied clinical manifestations of connective tissue disorders and their association with antinuclear antibodies in a tertiary care center. Indian Dermatol Online J. 2019; 10(4):413-7. doi:10.4103/idoj.IDOJ_398_18.
16. Niklas K, Niklas A, Mularek-Kubzdela T, Puszczewicz M. Prevalence of pulmonary hypertension in patients with systemic sclerosis and mixed connective tissue disease. Medicine (Baltimore). 2018; 97(28):e11437. doi:10.1097/MD.0000000000011437.
17. Jung JY, Lee CH, Kim HA, Choi ST, Lee JH, Yoon BY, et al. Pulmonary hypertension in connective tissue disease is associated with the New York Heart Association functional class and forced vital capacity, but not with interstitial lung disease. J Rheum Dis. 2018; 25(3):179-87. 10.4078/jrd.2018.25.3.17

Review Article

Association of Binge-Eating Disorders and Cardiovascular Diseases: A Literature Review

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ABSTRACT

Objective: To investigate the correlation between binge-eating disorders (BED) and cardiovascular diseases (CVD), synthesizing existing literature to identify risk factors and assess the extent of association.

Methodology: This review was conducted using PubMed, Cochrane Library, and Google Scholar, the primary database from January to October 2023. The search strategy included keywords related to BED, obesity, CVD, and eating habits. Only articles published within the past 12 years were considered. Inclusion criteria focused on studies assessing BED as a risk factor for CVD. Data extraction & synthesis were performed and the quality of included studies was assessed.

Results: The studies demonstrated a positive association between BED and various CVD outcomes, including hypertension, hyperlipidemia, and bradycardia. However, our results lacked numerical or categorical data representation.

Conclusion: This review provides compelling evidence supporting a direct link between BED and CVD, highlighting the increased risk of cardiovascular conditions independent of obesity. Lifestyle modifications and patient education are recommended interventions.

Keywords: *Cardiovascular diseases. Binge-eating disorder. Ischemic heart disease.*

INTRODUCTION

Binge-eating disorder is known for its multifactorial etiology and it is the most common eating disorder which can occur with obesity, psychological, physical, and mental comorbidities such as anxiety and depression.[1,2] Binge-eating disorder is defined as continuous episodes of eating without preventing weight gain through compensatory behaviors.[1] In the United States (US), the lifetime prevalence of BED is 2.6%.[2] The female-to-male ratio in BED is balanced, in contrast to other eating disorders. It is seen to be the most prevalent among older individuals, especially males.[3] There are many treatments for BED but the patient population seeking treatment is low. Currently, cognitive behavioral therapy (CBT) is a treatment of choice. It not only helps with the remission of binge-eating disorder but also improves associated general and specific psychopathologies.[4] Research has shown that BED is also associated with other medical comorbidities.[5,6]

According to a study conducted in 2015, about 1 in 3 people die globally due to cardiovascular diseases, and it is widely known that disease symptoms have a chronic onset starting in middle age. Obesity has been shown to be the most independent factor of all other risk factors which affect CVD.[7] In a cross-sectional study on Latinos to assess the high risk of CVD, it was concluded that there was an association between dysfunctional eating patterns and CVD metabolic risk factors.[8] The best way to manage CVD is to identify the risk factors, closely monitor them, introduce lifestyle changes, and involve a multidisciplinary team.[9]

The aim of the current study was to conduct a literature review to examine the association between binge-eating disorders and cardiovascular diseases. In addition, it would help synthesize existing literature for identifying risk factors, assessing the extent of the association, and contributing insights for informing future research and potential interventions in this context.

METHODOLOGY

In this literature review, electronic databases including PubMed, Cochrane Library, and Google Scholar, were systematically searched in January 2023. We thoroughly went through the articles and narrated the ones which showed a linkage between BED and CVD. Medical Subject Heading (MeSH) words and keywords used for search include binge-eating disorder, obesity, cardiovascular diseases, ischemic heart disease (IHD), coronary artery disease, eating habits, CVD and eating disorders, and cardiovascular disease risk factors. The number of articles found with each keyword are shown in Table 1 It is noteworthy that to guarantee the inclusion of thorough and robust findings, unpublished work and solitary abstracts were

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purposefully excluded from the study. To include current research and insights from the modern era, only complete publications published in the last 12 years were considered, in keeping with the study's scope.

The search was done on PubMed, Cochrane Library, and Google Scholar using the keywords: cardiovascular diseases, which showed 2842428 results, ischemic heart disease, which generated 551197 results, binge-eating disorders, which generated 5463 results, obesity, which generated 430082, eating habits which generated 213465, coronary artery disease which generated 189875, cardiovascular diseases and binge-eating disorders which generated 49 results.

Out of the 49 articles, 34 were excluded based on selection criteria (full-text and human). Out of 15 studies reviewed, 5 were irrelevant studies. In the end, 10 articles were included in the final analysis, all of which show a positive linkage between BED and CVD (Figure 1).

The study evaluated the relationship between binge-eating disorder and cardiovascular diseases, including hypertension, metabolic syndrome, and dyslipidemias. The analysis delved into the results obtained from the studies, providing insights into the association between BED and these cardiovascular conditions. Additionally, the manuscript discussed the potential implications of these findings for clinical practice and public health interventions aimed at managing both BED and cardiovascular diseases.

RESULTS

One of the included studies was a cross-sectional, correlational study with a sample of 111 patients with cardiovascular diseases, out of which binge-eating disorder was present in 18% of patients. So, this study showed a positive association between CVD and BED.[10] One of the review articles showed a strong association between BED and CVD.[11] Two studies suggested that mental illnesses including eating disorders are associated with hypertension and hypertriglyceridemia.[12,13] A cohort study in the USA with 350 participants of BED and 1875 controls scheduled for bariatric surgery analyzed that BED contributes to specific medical comorbidities in severely obese patients.[14] A study conducted in Spain in 2019 showed a positive link between bradycardia and all eating disorders including BED.[15] Moreover, a study done in Japan showed that eating disorders are associated with raised serum lipid levels.[16] Lastly, a study done in Sweden in 2016 showed a positive linkage between CVD and BED.[17]

According to an epidemiological data, patients with night eating syndrome were more likely to gain weight, become obese, and develop cardiometabolic diseases due to the consumption of large, mixed meals along with irregular sleep patterns.[18]

An analysis of a nationwide epidemiological database of around two million individuals without prior cardiovascular disease revealed that 51% of the general population had suboptimal eating habits. These habits were independently linked to a higher risk of CVD, including myocardial infarction, angina pectoris, stroke, and heart failure (Table 2).[19]

DISCUSSION

The current study investigated the association between BED and CVD using literature data. A study conducted by Garcia et al. in Spain revealed that compulsive overeating disorder was prevalent among cardiovascular disease patients, affecting 18% of them. It underscored the association between BED, body mass index, and anxiety, emphasizing the importance of a comprehensive evaluation of patients with cardiovascular conditions. The findings highlighted the importance of addressing both mental and physical health aspects in the care of these patients.[10] Another study reinforced that binge-eating disorder was linked with significant medical comorbidity beyond obesity alone. It emphasized the necessity for further investigation into the broader medical comorbidities associated with BED and how they intersected with obesity and concurrent psychiatric disorders.[11] A study done in the USA revealed independent associations between binge-eating disorder and comorbidities such as impaired glucose levels, high triglycerides, and urinary incontinence. Even after adjusting for demographic and health factors, BED remained linked to these conditions.[14]

Similarly, another study found that binge-eating disorder was associated with a wide range of diseases, with the strongest links observed for diabetes and circulatory system disorders, likely indicative of components of metabolic syndrome. Interestingly, individuals with BED who also had comorbid obesity were more likely to have a history of respiratory and gastrointestinal diseases compared to those without obesity. Importantly, the increased risk of certain somatic diseases in individuals with BED could not solely be attributed to obesity or other psychiatric comorbidities.[17]

Table 1: Search Results with Simple Keywords & MeSH Words

Keywords	Database	Number of Results
Binge-eating Disorder	PubMed/Google Scholar/Cochrane Library	5463
Obesity	PubMed /Google Scholar/Cochrane Library	430082
Cardiovascular Disease	PubMed/Google Scholar	2842428
Cardiovascular Risk Factors	PubMed/Google Scholar/Cochrane Library	275744
CVD and Eating Disorders	PubMed/Google Scholar/Cochrane Library	148
Cardiovascular Diseases and Binge-eating Disorder	PubMed/Google Scholar/Cochrane Library	49
Ischemic Heart Disease	PubMed/Google Scholar	551197
Coronary Artery Disease	PubMed/Google Scholar/Cochrane Library	189875
Eating Habits	PubMed/Google Scholar/Cochrane Library	213465

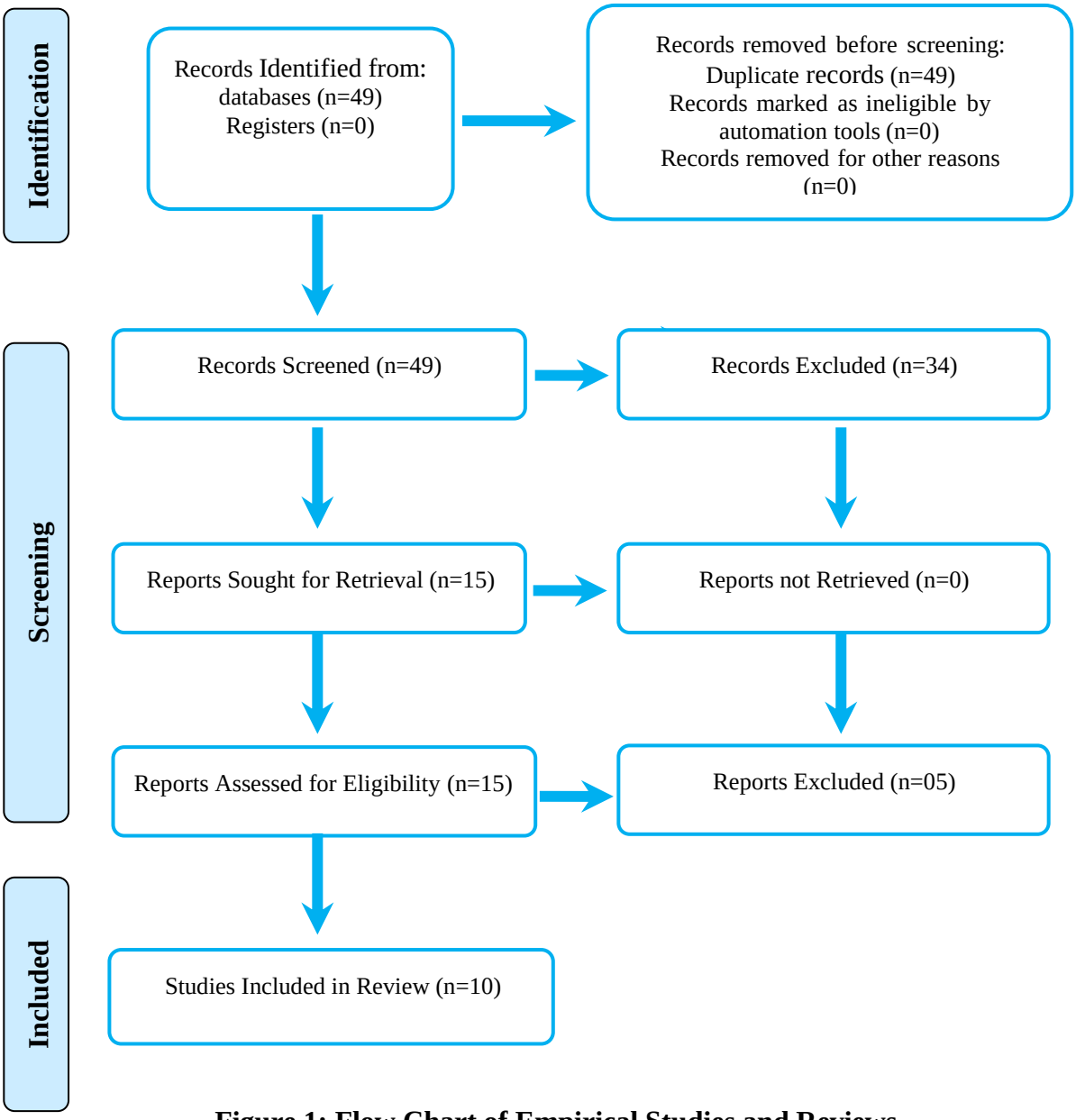

Figure 1: Flow Chart of Empirical Studies and Reviews

Table 2: Research Studies Correlating BED and CVD

Sr. No.	Author	Journal	Year	Country	Sample Population	Conclusion	Study Design
1	Kinsey et al. [18]	Nutrients	2015	USA	-	Consuming large meals at night time leads to obesity and cardiometabolic diseases	Review
2	Stein et al. [12]	Gen Hosp Psychiatry	2014	19 countries	52,095 adults from 19 countries	Most mental illnesses, including eating disorders, are associated with hypertension	Cross-sectional
3	Solmi et al. [13]	Acta Psychiatr Scand	2021	Brazil	13,388 participants	Researcher shows an increased risk of hypertriglyceridemia and hypertension in binge-eating individuals	Cohort
4	Garcia et al. [10]	Rev Lat Am Enfermagem	2018	Spain	111 patients with cardiovascular diseases	There is a positive linkage between BED and CVD	Cross-sectional, correlational
5	Kaneko et al. [19]	Atherosclerosis	2021	Japan	1941125	The findings underscore the importance of optimal eating behaviors for the primary prevention of CVD	Cross-sectional
6	Thornton et al. [17]	Int J Eat Disord	2016	Sweden	850 cases with BED	BED is associated with a risk of circulatory system diseases	Case-control
7	Mitchell et al. [14]	Int J Eat Disord	2015	USA	2225 Bariatric surgery candidates	BED contributes to specific medical comorbidities in severely obese patients	Prospective Case-control
8	Olguin et al. [11]	Eat Weight Disord	2016	NA	Patients with BED	There is an association between BED and CVD	Narrative review
9	Marin et al. [15]	Rev Med Chil	2019	Spain	53 women	There's a link between bradycardia and all eating disorders, including BED	Cross-sectional descriptive
10	Nakai et al. [16]	Intern Med	2016	Japan	732 Japanese women with eating disorders	Eating disorders are associated with raised serum lipid levels	Cohort

A cross-sectional study conducted in 19 countries revealed significant associations between various psychiatric disorders and the subsequent diagnosis of hypertension, even after adjusting for psychiatric comorbidity. Specifically, depression, panic disorder, social phobia, specific phobia, binge-eating disorder, bulimia nervosa, alcohol abuse, and drug abuse were all linked to hypertension.[12]

A study showed that individuals who engaged in binge-eating had a higher likelihood of developing metabolic syndrome due to elevated body mass index (BMI). Furthermore, they faced increased risks of hypertriglyceridemia and hypertension, even when considering factors other than BMI. These findings suggested potential causal relationships between binge-eating behavior and metabolic health issues.[13] Another study by Nakai et al. aimed to evaluate risk factors for cardiovascular diseases in different groups of feeding and eating disorders by investigating lipid abnormalities in a large Japanese cohort. Participants included 732 women with anorexia nervosa, bulimia nervosa, and BED. The study highlighted the presence of elevated low-density lipoproteins cholesterol and non-high-density lipoprotein cholesterol levels across all eating disorder groups, suggesting an increased risk of cardiovascular diseases, particularly considering the chronic nature of these conditions.[16]

A study carried out in Spain demonstrated a positive correlation between bradycardia and all eating

disorders, including BED.[15] Large, mixed meals and inconsistent sleep patterns were associated with increased risk of weight gain, obesity, and cardiometabolic diseases in individuals with night eating syndrome, according to a study done in the United States.[18]

A countrywide epidemiological database containing almost two million people who had never had cardiovascular illness was used in another Japanese study, which found that 51% of the general population had unhealthy eating habits. An increased risk of CVD, which includes myocardial infarction, angina pectoris, stroke, and heart failure, has been independently associated to these practices.[19]

Genetic links between BED and CVD exist. Shared deoxyribonucleic acid (DNA) methylation suggests BED as a risk factor for CVD.[20,21] Following an eating routine and losing weight are key predictive factors for dietary issues which have been displayed to influence DNA methylation designs across different body tissues.[22] Understanding epigenetics gives an open door with respect to therapeutic and diagnostic platforms; this makes it easier to come up with ways to treat the disease and properly screen for people at high risk.[23,24]

Many changes in diet, medicines, alcohol use, and smoking can act as a stressor in triggering CVD.[25] However, minority status, deprivation, violence, trauma, and major mental health illnesses are possible risk factors for binge-eating disorder. An unhealthy diet is a risk factor for both BED and CVD as it influences binge-eating and eventually is a cause of cardiovascular disorders.[26] Another particular risk factor identified in eating disorders is the cultural pressure for a thinner appearance.[27] Smoking cessation, diet therapy, and exercise therapy are all lifestyle modifications enlisted in Japan's Atherosclerotic Cardiovascular Disease guidelines for disease prevention.[28] Progression and development of peripheral arterial disease (PAD) and complications, including major adverse cardiovascular events and major adverse limb events, are shown to be affected by dietary patterns and eating disorders. Obesity is an important risk factor of PAD. It results from BED response to distress and discomfort that leads to recurrent episodes of overeating with resultant weight gain.[29]

Aging is a significant risk factor and a leading cause of death in CVD.[22] Binge-eating disorder and CVD are both prevalent in children and adolescents, causing physical and mental health problems. The peak age of BED onset is late adolescence, and childhood obesity is a significant factor in the development of CVD during adolescence. To further cement such a claim, childhood obesity according to the above-given literature has a significant role to play in the development of adolescent CVD and BED. Although evidence suggests that BED is more common in females, it is, in reality, highest in males.[30,31] On the other hand, cardiovascular diseases have a chronic onset starting in middle age, it is pertinent to shed light on the fact that BED, according to the published literature is most prevalent in older individuals. Aging leads to uniform and generalized structural degeneration and functional decline, even if different cardiovascular system components may be affected quite heterogeneously. Furthermore, as discussed above, obesity is the most independent risk factor affecting cardiovascular diseases, thus serving as a pathological bridge between CVD and BED. Enough evidence shows that overweight/obese people and sexual minorities are more likely to meet the diagnostic criteria of disordered eating than heterosexuals and people having normal BMI/smaller bodies.[32] Binge-eating disorder and night eating syndrome are associated with obesity, increased risk of metabolic dysfunction, psychopathology, and various treatment options including CBT and selective serotonin reuptake inhibitors.[33]

CONCLUSION

Following a thorough examination of prior studies, we established a direct link between cardiovascular diseases and binge-eating disorders. Studies also revealed a higher incidence of hypertension, hyperlipidemia, and hypertriglyceridemia, irrespective of obesity, in individuals with eating disorders. Consequently, BED should be recognized as a risk factor for cardiovascular diseases. Physicians should advise lifestyle modification to their patients and educate them about this association.

STRENGTHS & LIMITATIONS

A main limitation to this review is the small number of available studies. That's why we incorporated studies of all qualities which affect the robustness of our findings. The manuscript "Binge-eating Disorder and Cardiovascular Diseases" underwent a risk of bias assessment to ensure the reliability of its findings. Selection bias was scrutinized to ascertain if the sample adequately represented individuals with binge-eating disorder and cardiovascular diseases. Measurement bias was evaluated concerning the methods used to measure BED, CVD, and associated risk factors, ensuring their

validity. Confounding bias was addressed by assessing the control of potential confounding variables, such as age, sex, and comorbidities, in the analysis. Reporting bias was considered to ensure transparent reporting of all relevant data, including negative findings. Publication bias was also scrutinized to determine if only significant results were included, potentially skewing the overall conclusion. These assessments aimed to enhance the integrity and reliability of the manuscript's conclusion regarding the relationship between BED and CVD. Heterogeneity among included studies, such as differences in populations, interventions, and outcomes, may limit the ability to draw definitive conclusions.

RECOMMENDATIONS

Based on our findings in this review, we recommend awareness programs on binge-eating disorders. Physicians should advise lifestyle modifications, especially regarding a healthy diet to their patients and educate them while offering CBT as the treatment of choice for binge-eating disorders. Further research addressing identified deficiencies is warranted to enhance understanding and inform clinical practice.

Authors' Contributions:
F.T: Results, methodology, and discussion
U.B.Z: Results, Prisma, and abstract
F.I: Critical revision and final approval of the draft
I.M: Supervision
M.S.H: Introduction and conclusion
M.A.L: Formatting and abstract

REFERENCES

1. Hilbert A. Binge-eating disorder. Psychiatr Clin North Am. 2019; 42(1):33-43. doi:10.1016/j.psc.2018.10.011.

2. Guerdjikova AI, Mori N, Casuto LS, McElroy SL. Binge-eating disorder. Psychiatr Clin North Am. 2017; 40(2):255-66. doi:10.1016/j.psc.2017.01.003.

3. Smink FR, van Hoeken D, Hoek HW. Epidemiology of eating disorders: incidence, prevalence and mortality rates. Curr Psychiatry Rep. 2012; 14(4):406-14. doi:10.1007/s11920-012-0282-y.

4. Aguera Z, Lozano-Madrid M, Mallorqui-Bague N, Jimenez-Murcia S, Menchon JM, Fernandez-Aranda F. A review of binge-eating disorder and obesity. Neuropsychiatr. 2021; 35(2):57-67. Doi:10.1007/s40211-020-00346-w.

5. Olguin P, Fuentes M, Gabler G, Guerdjikova AI, Keck PE Jr, McElroy SL. Medical comorbidity of binge-eating disorder. Eat Weight Disord. 2017; 22(1):13-26. doi:10.1007/s40519-016-0313-5.

6. Wassenaar E, Friedman J, Mehler PS. Medical complications of binge-eating disorder. Psychiatr Clin North Am. 2019; 42(2):275-86. doi:10.1016/j.psc.2019.01.010.

7. Jokinen E. Obesity and cardiovascular disease. Minerva Pediatr. 2015; 67(1):25-32. Available from: https://pubmed.ncbi.nlm.nih.gov/25387321.

8. Lopez-Cepero A, Frisard CF, Lemon SC, Rosal MC. Association of dysfunctional eating patterns and metabolic risk factors for cardiovascular disease among Latinos. J Acad Nutr Diet. 2018; 118(5):849-56. doi:10.1016/j.jand.2017.06.007.

9. Francula-Zaninovic S, Nola IA. Management of measurable variable cardiovascular disease risk factors. Curr Cardiol Rev. 2018; 14(3):153-63. doi:10.2174/1573403X14666180222102312.

10. Garcia GD, Pompeo DA, Eid LP, Cesarino CB, Pinto MH, Gonçalves LWP. Relationship between anxiety, depressive symptoms and compulsive overeating disorder in patients with cardiovascular diseases. Rev Lat Am Enfermagem. 2018; 26:e3040. doi:10.1590/1518-8345.2567.3040.

11. Olguin P, Fuentes M, Gabler G, Guerdjikova AI, Keck PE Jr, McElroy SL. Medical comorbidity of binge-eating disorder. Eat Weight Disord. 2017; 22(1):13-26. doi:10.1007/s40519-016-0313-5.

12. Stein DJ, Aguilar-Gaxiola S, Alonso J, Bruffaerts R, de Jonge P, Liu Z, et al. Associations between mental disorders and subsequent onset of hypertension. Gen Hosp Psychiatry. 2014; 36(2):142-9. doi:10.1016/j.genhosppsych.2013.11.002.

13. Solmi F, Moreno AB, Lewis G, Angelica Nunes M, de Jesus Mendes da Fonseca M, et al. Longitudinal association between binge-eating and metabolic syndrome in adults: Findings from the ELSA-Brasil cohort. Acta Psychiatr Scand. 2021; 144(5):464-74. doi:10.1111/acps.13356.

14. Mitchell JE, King WC, Pories W, Wolfe B, Flum DR, Spaniolas K, et al. Binge-eating disorder and medical comorbidities in bariatric surgery candidates. Int J Eat Disord. 2015; 48(5):471-6. doi:10.1002/eat.22389.

15. Marin B V, Rybertt V, Briceno AM, Abufhele M, Donoso P, Cruz M, et al. [Female adolescents with eating disordes: cardiac abnormalities]. Rev Med Chil. 2019; 147(1):47-52. doi:10.4067/S0034-98872019000100047.

16. Nakai Y, Noma S, Fukusima M, Taniguchi A, Teramukai S. Serum lipid levels in patients with eating disorders. Intern Med. 2016; 55(14):1853-7. doi:10.2169/internalmedicine.55.5632.

17. Thornton LM, Watson HJ, Jangmo A, Welch E, Wiklund C, von Hausswolff-Juhlin Y, et al. Binge-eating disorder in the Swedish national registers: somatic comorbidity. Int J Eat Disord. 2017; 50(1):58-65. doi:10.1002/eat.22624.

18. Kinsey AW, Ormsbee MJ. The health impact of nighttime eating: old and new perspectives. Nutrients. 2015; 7(4):2648-62. doi:10.3390/nu7042648.

19. Kaneko H, Itoh H, Kiriyama H, Kamon T, Fujiu K, Morita K, et al. Possible association between eating behaviors and cardiovascular disease in the general population: analysis of a nationwide epidemiological database. Atherosclerosis. 2021; 320:79-85. doi:10.1016/j.atherosclerosis.2021.01.022.

20. Hubel C, Marzi SJ, Breen G, Bulik CM. Epigenetics in eating disorders: a systematic review. Mol Psychiatry. 2019; 24(6):901-15. doi:10.1038/s41380-018-0254-7.

21. Shi Y, Zhang H, Huang S, Yin L, Wang F, Luo P, et al. Epigenetic regulation in cardiovascular disease: mechanisms and advances in clinical trials. Signal Transduct Target Ther. 2022; 7(1):200. doi:10.1038/s41392-022-01055-2.

22. Ling C, Ronn T. Epigenetics in human obesity and type 2 diabetes. Cell Metab. 2019; 29(5):1028-44. doi:10.1016/j.cmet.2019.03.009.

23. Booij L, Steiger H. Applying epigenetic science to the understanding of eating disorders: a promising paradigm for research and practice. Curr Opin Psychiatry. 2020; 33(6):515-20. doi:10.1097/YCO.0000000000000632.

24. van der Harst P, de Windt LJ, Chambers JC. Translational perspective on epigenetics in cardiovascular disease. J Am Coll Cardiol. 2017; 70(5):590-606. doi:10.1016/j.jacc.2017.05.067.

25. Bays HE, Taub PR, Epstein E, Michos ED, Ferraro RA, Bailey AL, et al. Ten things to know about ten cardiovascular disease risk factors. Am J Prev Cardiol. 2021; 5:100149. doi:10.1016/j.ajpc.2021.100149.

26. Bray B, Bray C, Bradley R, Zwickey H. Binge-eating disorder is a social justice issue: a cross-sectional mixed-methods study of binge-eating disorder experts' opinions. Int J Environ Res Public Health. 2022; 19(10):6243. doi:10.3390/ijerph19106243.

27. Hu C, Zhang X, Teng T, Ma ZG, Tang QZ. Cellular senescence in cardiovascular diseases: a systematic review. Aging Dis. 2022; 13(1):103-28. doi:10.14336/AD.2021.0927.

28. Kinoshita M, Yokote K, Arai H, Iida M, Ishigaki Y, Ishibashi S, et al. Japan atherosclerosis society (JAS) guidelines for prevention of atherosclerotic cardiovascular diseases 2017. J Atheroscler Thromb. 2018; 25(9):846-984. doi:10.5551/jat.GL2017.

29. Cecchini AL, Biscetti F, Rando MM, Nardella E, Pecorini G, Eraso LH, et al. Dietary risk factors and eating behaviors in peripheral arterial disease (PAD). Int J Mol Sci. 2022; 23(18):10814. doi:10.3390/ijms231810814.

30. Bohon C. Binge-eating disorder in children and adolescents. Child Adolesc Psychiatr Clin N Am. 2019; 28(4):549-55. doi:10.1016/j.chc.2019.05.003.

31. Parsanathan R, Jain SK. Novel invasive and noninvasive cardiac-specific biomarkers in obesity and cardiovascular diseases. Metab Syndr Relat Disord. 2020; 18(1):10-30. doi:10.1089/met.2019.0073.

32. Beccia AL, Baek J, Austin SB, Jesdale WM, Lapane KL. Eating-related pathology at the intersection of gender identity and expression, sexual orientation, and weight status: an intersectional multilevel analysis of individual heterogeneity and discriminatory accuracy (MAIHDA) of the growing up today study cohorts. Soc Sci Med. 2021; 281:114092. doi:10.1016/j.socscimed.2021.114092.

33. McCuen-Wurst C, Ruggieri M, Allison KC. Disordered eating and obesity: associations between binge-eating disorder, night-eating syndrome, and weight-related comorbidities. Ann N Y Acad Sci. 2018; 1411(1):96-105. doi:10.1111/nyas.13467.

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