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The Dire Need to Include Leadership Education in the Medical School Curriculum

Prof Faisal Aziz
Head of Vascular Surgery Penn State University USA
DOI:*https://doi.org/10.51273/esc22.25182-editorial*

The medical education curriculum is traditionally designed to educate the students about the fundamentals of basic and clinical medical sciences. For centuries, the educational curriculum has produced excellent physicians. With increasing focus on healthcare delivery over the past few decades, physicians have learned that while traditional education has successfully made outstanding clinicians, it has failed to prepare them for healthcare delivery challenges. As a result, healthcare executives worldwide have filled the vacuum in healthcare leadership. According to a recent survey, less than 5% of healthcare chief executive officers in the US are physicians[1]. It has been increasingly recognized that the healthcare business differs from other markets as it involves empathy for ailing humanity. There has been an increasing number of physicians who feel less satisfied with their jobs. Unless and until physicians are part of the decision-making processes in healthcare delivery, we will continue to have a dilemma of unsatisfied physicians and patients. In my opinion, the fundamental flaw of current medical education is that it does not educate medical students about basic leadership principles. To meet the needs of twenty-first-century healthcare, we need physicians who can provide excellent clinical care to our patients and possess the ability to navigate the increasingly complex landscape of healthcare and lead the unmet needs of healthcare delivery. In short, we are producing physicians, while the world needs physician leaders. I would argue that physicians already possess innate needs for leadership. Integrity is the cornerstone of leadership, and society considers physicians to have the highest degree of integrity among all educated professionals. After all, the community members trust us with the decisions that impact their lives and health! Physicians, by nature, are empathic people and bring out the humanistic side of leadership. Our patients, their families, and society trust us to make decisions for their health. It is only natural to consider physicians leading the way in ensuring concise and impactful healthcare delivery. While the traditional medical system was structured in a hierarchical manner, modern-day health systems increasingly rely on teamwork, where every healthcare team member is an asset and treated with the same degree of respect. The healthcare teams include physicians, nurses, physical therapists, occupational therapists, and pharmacists, among many other allied healthcare practitioners. In general, physicians are considered leaders of healthcare teams. Physicians of the current day and age need to work with other healthcare team members effectively to deliver the best possible care to their patients[2]. Physicians in leadership roles must collaborate with hospital administrators to ensure a conducive professional environment where physicians and patients can feel safe and satisfied. We need to train future physicians in the basic principles of leadership with practical communication skills. The next question is, how do we achieve this goal? We need to include leadership education in the medical school curriculum. To make it effective, we should not grade students in this course. In my medical school years, I felt that any system requiring examinations or grades was a burden. We do not want to increase the burden on already "studied-out" medical students. The leadership course should be more of an optional, fun activity so that only those students who are interested in pursuing leadership roles in their careers can be a part of it. We should also ensure that for the interested students, there are ample resources for leadership education. It should include lectures on

leadership essentials, conversations with healthcare leaders, and shadowing healthcare executives to understand the scope of the healthcare issues we face and the soft skills required to handle these complicated dilemmas. We should carefully analyze this leadership curriculum's impact on medical students' careers and then make modifications as deemed necessary. We should encourage an environment where leadership courses are more in the format of open dialogue, where students can ask questions without any fear. We have an excellent opportunity to train a crop of physician leaders of the future who will not only be able to provide excellent clinical care to our patients but also lead the process of healthcare delivery in healthcare systems of the future!

References

1. Kay B. An Antidote for burnout: Vascular Surgeons as Hospital Administrators. Vascular Specialist. June 23, 2022. https://vascularspecialistonline.com/an-antidote-for-burnout-vascular-surgeons-as-hospital-administrators/
2. Stoller JK, Goodall A and Baker A. Why the best hospitals are managed by doctors. Harvard Business Review. December 27, 2016. https://hbr.org/2016/12/why-the-best-hospitals-are-managed-by-doctors

Safety and Efficacy of Balloon Remodeling Technique for Treating Cerebrovascular Aneurysms

Qasim Bashir,[1] Faisal Farooq,[2] Asim Ishfaq,[3] Javed Iqbal,[4]

Abstract

Objective: To assess the safety and efficacy of Balloon remodeling technique (BRT) for coil placement in Pakistani patients with wide neck cerebral aneurysms.

Method: This study included a total of 39 patients (23 females and 16 males) treated with BRT for 44 cerebral aneurysms over a period of six years, at Hameed Latif Hospital, Lahore. Characteristics of aneurysms were analyzed, and complications, occlusion rates, and outcomes were ascertained for relevant comparisons with the available literature on Balloon Remodeling Technique.

Results: Overall, 35 (79.5%) patients presented with ruptured aneurysms and 37 of the 44 aneurysms (84.1%) were located within the anterior circulation. The remodeling technique was successful in achieving complete or near complete occlusion of 39 of total 42 treated aneurysms (92.9%). Two procedures were aborted due to intraoperative complications. The rate of technical success achieved was 95.4%. Treatment related complications were seen in four cases (9.5%) and included intra-procedural aneurysmal ruptures and thromboembolic phenomena.

Conclusion: Balloon Remodeling Technique can achieve high rates of aneurysm occlusion with low rates of complications and is a good option for treatment of both ruptured and unruptured wide neck cerebral aneurysms in our population.

Keywords: intracranial aneurysm, endovascular procedures, balloon remodeling technique, Pakistan.

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Introduction

Neuroendovascular management of intracranial aneurysms is a minimally invasive technique. Since its introduction, it has replaced more invasive surgical clipping of the same aneurysms.[1] However, aneurysms with wide necks are not amenable to conventional endovascular coil placement due to high risk of coil protrusion into the parent vessel. Balloon remodeling technique (BRT), initially described by Moret et al.[2] in 1994, offers an alternative solution for the endovascular coiling of such cerebral aneurysms, and ever since then its usage has been on the rise. Commonly used acronyms for this technique include; BRT (Balloon Remodeling Technique),[3] BACE (Balloon-assisted Coil Embolization)[4] and BAC (Balloon-assisted Coiling).[5,6]

Historically, wide neck cerebral aneurysms are defined as those in which the neck of an aneurysm is ≥4 mm, or when the dome to neck ratio is ≤2.[2,3,7] Briefly, BRT is performed using a non-detachable balloon that is inflated intermittently in front of the neck of an aneurysm at the time of each coil placement. The inflated balloon allows easy configuration of the coils inside the aneurysm dome and prevents their displacement into the parent vessel. It is removed at the end of the coil placement procedure.[4,8]

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Coil placement with BRT offers a higher rate of aneurysm occlusion and anatomic efficacy, offering at the same time a similar safety as the standard endovascular coiling.[9] This technique is frequently used in the treatment of both ruptured and unruptured aneurysms.[6,8,10] Over the years, in addition to being employed for sidewall aneurysms, this technique has also been used to treat aneurysms with complex origins, such as bifurcation or basilar apex aneurysms.[3,6]

Efficacy of BRT is judged from the aneurysm occlusion rates, whereas its safety from the rates of complications, as well as post-operative morbidity and mortality.[6,8,10] Most common complications encountered in BRT include thromboembolic and hemorrhagic phenomenon.[9,11-14] Previous BRT studies have reported 2.1 to 7.7% rates of hemorrhagic, whereas 4.5 to 7.1% rates of thromboembolic phenomenon.[8,10,15]

This technique has only recently seen the doors to this country and studies indicative of its application in Pakistan have been lacking.[16] Our initial experience from four patients that underwent BRT in the same setting was reported in our previous study.[16] The objective of present study is to establish the safety and efficacy of this technique in Pakistani population by presenting the findings of our data of six years, with relevant comparisons of our outcomes with those reported in other BRT studies.

Material and Methods

Approval for this retrospective study was granted by the institutional ethical review committee of Hameed Latif Hospital, Lahore. Using OpenEpi (version 3.0), a minimum sample size of 39 was considered to be appropriate with a confidence interval of 95%. A retrospective review of the patient medical records, procedure notes, and angiograms was performed to collect data on patient demographics, degree of aneurysm occlusion, and any procedural complications (Table 1). A total of 39 patients harboring 44 wide neck cerebral aneurysms were selected. These patients had received treatment with BRT between December, 2013 to June, 2020, in the dedicated neuroendovascular angiographic suite of Hameed Latif Hospital, Lahore.

The inclusion criteria were that the patients should have been diagnosed with ruptured or unruptured wide neck cerebral aneurysm via cerebral CT angiography, must have been selected for neuroendovascular treatment with BRT via a consensus among institutional multidisciplinary team, comprising of neurology, neurosurgery, and neuroendovascular surgery departments, should have no history of bleeding diathesis or thrombophilia, and no history of any previous aneurysm treatment.

The degree of aneurysm occlusion was defined using a modified three-point scale comprising complete occlusion, near-complete occlusion (neck remnant), and incomplete occlusion (aneurysm or sac remnant) [7,17]. An aneurysm was graded as wide neck if the neck was 4 mm or greater and/or fundus-to-neck ratio <2.0 on digital subtraction angiography[2,3,7]. Cerebral aneurysms were broadly classified based on their location (basilar apex, other posterior fossa locations, anterior cerebral artery (ACA), anterior communicating artery (Acom), middle cerebral artery (MCA), or internal carotid artery (ICA)) and geometry i.e. originating either from a side wall or bifurcation/trifurcation (Table 2). None of the patients received pre-procedure antiplatelet therapy.

Statistical calculations were performed using SPSS version 21 (IBM, Chicago, IL, USA). Specific variables that were analyzed included age, gender, aneurysm location, aneurysm size, use of BRT, and aneurysm rupture status. Additional patient data collected included degree of aneurysm occlusion after coil placement and BRT related complications (i.e. thromboembolic events & ruptures).

All procedures were performed by using transfemoral access in a dedicated single plane Toshiba Japan Infinix 8000 Angiography suite under general anesthesia after obtaining informed patient consent. Briefly, after routinely obtaining femoral access using a 6F introducer sheath, all patients were administered 5000U of intravenous heparin followed by measurement of activated clotting time (ACT) after 10 minutes post administration. An additional 1000U bolus of intravenous heparin was administered every hour for the duration of the procedure. The systemic heparinization was adjusted to maintain the ACT between 250-300 seconds. Various 6Fr guiding catheters were used in our patients (Chaperone, Microvention, Tustin, CA, USA; Primum MPC, PendraCare International, Leek, Groningen, The Netherlands) and depending upon the aneurysm location, they were placed either in the ipsilateral internal carotid or the dominant vertebral artery. Both the microcatheter and the balloon catheter were coaxially placed through the guide catheter. HyperForm, HyperGlide (Medtronic, Minneapolis, MN, USA), Ascent (Cerenovus, Irvine, CA, USA), Sceptor C, and Sceptor XC (Microvention, Tustin, CA, USA) remodeling balloons were used (Table

1). In sidewall aneurysms, the balloon was placed directly across the neck of the aneurysm (Figure 1-2). In bifurcation aneurysms, such as basilar apex and carotid terminus aneurysms, a longer balloon length was used and balloon inflated sufficiently to completely cover the aneurysm neck. Balloons were inflated for initial framing of the coil, to prevent prolapse of the coil into the parent vessel, and for dense packing of the last coil. The balloons were removed after procedure was completed. Both balloon inflation and deflation were performed under direct fluoroscopic visualization to ensure that there was no over inflation or migration of the coil out of the neck before detachment. Control angiography runs were routinely obtained after each coil deployment to assess residual filling in an aneurysm and identify any thrombus formation adherent to the coil mass or within the parent vessel adjacent to the aneurysm neck. If thrombus formation was noted, an immediate ACT was measured followed by a loading dose of intravenous Tirofiban (4cc×25mcg=1mg). Post procedure, the groin sheath in such patients was sutured to the skin and attached to continuous non-heparinized saline infusion usually at 0.10mcg/kg/min for 8-12 hours. All patients were extubated in the neuroangiography suite and then monitored in intensive care unit for a minimum of 24 hours.

Results

The remodeling technique was performed in 39 patients (mean age 45.2 ± 11.9) harboring 44 aneurysms. Of the 44 aneurysms, 37 (84.1%) were located within the anterior circulation. Morphologically, 26 (59%) aneurysms originated from a sidewall and the rest (40.9%) from either a bifurcation or a trifurcation (Table 2). Majority of the aneurysms were ruptured (79.5%). (Table 1). Technical success was achieved in 42 of the 44 (95.4%) aneurysms and the BRT failure rate was 4.6% (Table 3). In two of the 44 patients, the procedure was aborted because one of them had a wider than calculated aneurysm neck, and thus making BRT impossible, whereas the other patient experienced worsening of the feeding artery spasm upon introduction of the micro-catheter and the balloon catheter.

The initial rates of aneurysm occlusion, as seen on post-procedure angiograms, were complete occlusion in 17 (40.5%) patients, near-complete in 22 (52.4%) patients, and incomplete in 3 (7.1%) patients (Table 3). The remaining three incompletely occluded aneurysms had progressed to complete occlusion at 6 months as ascertained by MR angiography.

Of the 42 aneurysms successfully treated with BRT, treatment related complications were seen in four procedures (9.5%). There were two instances of aneurysm rupture during coil placement in two patients, and thromboembolic phenomena requiring intravenous Tirofiban in two others. Post procedure, no new deficits were identified in any of the four patients.

Table 1: *Patient Demographics*

Total Patients	**39**	
Total Aneurysms	44	
Mean Age (years)	45.23 ± 11.96	
Gender	Femle	23
	Male	16
Indications	A. Ruptured:	
	SAH	31
	ICH	4
	B. Un-ruptured:	
	Headache	3
	Aneurysm re-growth	1
Balloon Used	Hyper Glide	19
	Hyper Form	09
	Ascent Occlusion	05
	Scepter C	05
	Scepter XC	01

SAH= Subarachnoid Hemorrhage,
ICH = Intracerebral Hemorrhage

Table 2: *Aneurysm Morphology & Locations (N=44)*

Sidewall Aneurysms (*n*=26)*		**Bifurcation/Trifurcation Aneurysms (*n*=18)***	
Paraophthalmic ICA	1 (3.8)	ACA-Acom junction	4 (22.2)
Supraclinoid ICA	7 (26.9)	MCA trifurcation	2 (11.1)
Paraclinoid ICA	1 (3.8)	MCA bifurcation	8 (44.4)
Cavernous ICA	1 (3.8)	Vertebral Artery - PICA junction	1 (5.5)
ACA	1 (3.8)	PCA-SCA junction	1 (5.5)
Acom	5 (19.2)	Basilar apex	1 (5.5)
MCA	5 (19.2)	Carotid Terminus	1 (5.5)
PCA	1 (3.8)		
Fetal PCA/Pcom	1 (3.8)		
Pcomm	2 (7.7)		
Vertebral Artery	1 (3.8)		

*Data are number of patients. Numbers in parenthesis are percentages.
ACA = anterior cerebral artery, Acom = anterior communicating artery, ICA = internal carotid artery,
MCA = middle cerebral artery, PCA = Posterior cerebral artery, Pcom = posterior communicating artery,
PICA = posterior inferior cerebellar artery, SCA = superior cerebellar artery

Table 3: *Final Outcomes of BRT*

Technical Success (n=44)	**95.4%**	
Failure Rate (n=44)	4.6 %	
Morphological Outcome (n=42)	Initial occlusion:	
	Complete	17 (40.5%)
	Neck Remnant	22 (52.4%)
	Aneurysm Remnant	03 (7.1%)
Procedural Complications (n=42)	Rupture (asymptomatic)	02 (4.8%)
	Thromboembolic (asymptomatic)	02 (4.8%)

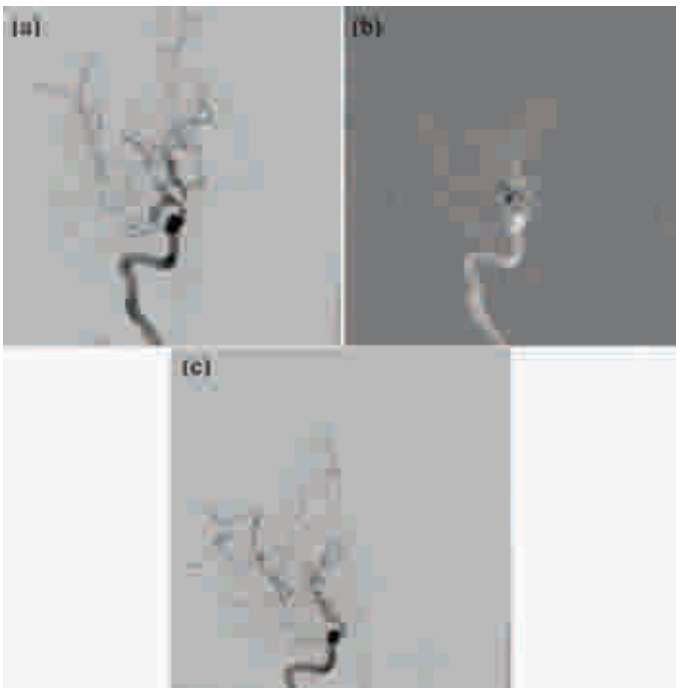

Fig-1: *A 48-year-old female with ruptured right supraclinoid ICA aneurysm. (a) Right carotid angiography showing a saccular inferiorly directed supraclinoid ICA aneurysm with a distal sac attached to a stem. BRT was thought appropriate to completely occlude the stem without smaller coils protruding into the parent ICA. (b) Road map image showing microcatheter tip within the aneurysm and last coil being deployed with inflated balloon mounted microcatheter across the aneurysm neck. (c) Post Balloon-Assist Coil placement, complete obliteration of the aneurysm achieved without compromising the fetal right posterior cerebral artery origin.*

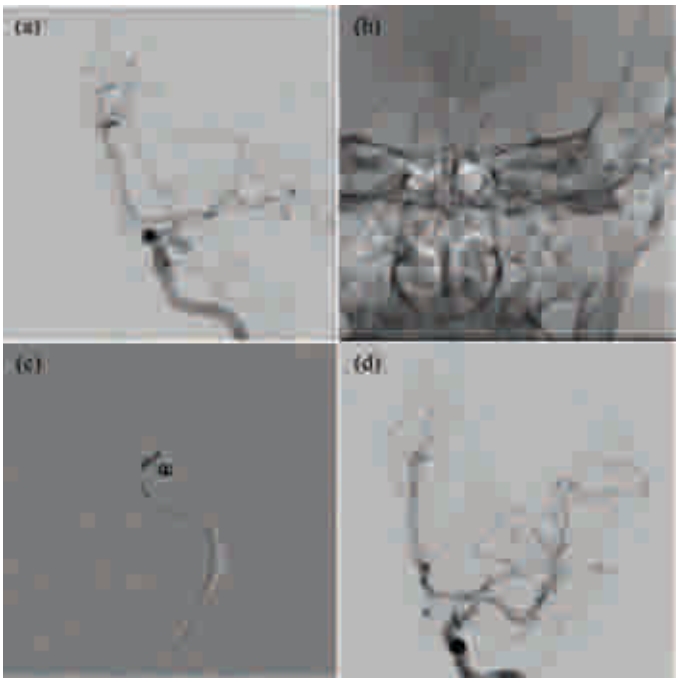

Fig-2: *A 50-year-old male with ruptured fetal left posterior cerebral artery aneurysm. (a) Note inferiorly directed relatively wide neck aneurysm. At this location with no proximal bridging, at times the last few coils can protrude into the parent vessel. (b) Native image showing distal marker of the microcatheter within the aneurysm dome and two markers of the balloon microcatheter across the aneurysm neck. (c) Road map Image showing coil placement in progress with balloon inflated. (d) Post balloon-assist coil placement control angiography demonstrates complete aneurysm occlusion and patency of fetal left PCA.*

Discussion

This study presents a retrospective single operator two-center analysis in a consecutive series of 44 patients with both ruptured and unruptured cerebral aneurysms undergoing BRT. It shows procedural safety in terms of anatomical efficacy and perioperative complications. In this series, overall initial anatomic results in patients treated with remodeling technique were very good with complete occlusion in 40.5% patients, near-complete in 52.4%, and incomplete in 7.1% of them. Thus, adequate occlusion (complete to near-complete) with BRT was seen in 92.9% of the patients. During the follow-up period (range: 3-12 months), no patient required further treatment or developed a recurrent aneurysm neck or lumen. These results are comparable to those reported

in a large prospective, multicenter CLARITY[8] study looking at only ruptured intracranial aneurysms, whereby the occlusion rates in the remodeling group with wide neck aneurysms were complete occlusion in 50.0% of cases, a neck remnant in 44.9%, and an aneurysm remnant in 5.1% of them. Similarly, ATENA[10] looking at outcomes of BRT in unruptured aneurysms reported the occlusion rates to be complete occlusion in 59.8% of the aneurysms and a neck remnant in 20.1% of them. Consoli et al[18] in their study of BRT in 164 patients, reported complete occlusion in 78% cases and near-complete in 14.6% of them. Similar results were reported by Gentric et al,[15] wherein an adequate occlusion rate (complete to near-complete) of 92.1% was achieved.

Present study showed the rate of peri-operative complications to be 9.5%, with 4.8% being thromboembolic in nature and the remaining (4.8%) being hemorrhagic. CLARITY,[8] showed that the remodeling group had thromboembolic events in 10 of the 52 (19%) cases, and intra-operative rupture in four of them (7.7%). Whereas, ATENA[10] showed the former in 7.1% patients, and the latter in 2.6% of them. Similarly, the rate of thromboembolic phenomenon reported by Consoli et al[18] was 0.6% and that of hemorrhagic phenomenon 4.6%. Dabus et al11 included 84 BRT-treated cerebral aneurysms in their study, and reported 3% thromboembolic and 6% hemorrhagic events.

Long-term outcomes of this technique have shown that it is a feasible option for both ruptured and unruptured cerebral aneurysms located in all locations.[6,9,19] The BRT failure rate of 4.6% in this study is in line with that reported by Consoli et al[18] of 1.2% and that by Cottier et al of 8%.[20] Common reasons for failure include completely unfavorable dome-to-neck ratio resulting in wider neck and rendering it difficult to form a stable coil mass configuration, tortuous cervical and intracranial vasculature limiting multiple microcatheter access, vessel going in spasm, and acute angle of the parent vessel e.g. paraophthalmic aneurysm location. In this study, clinical outcomes were favorable in all patients. However, the rates of treatment related morbidity and mortality were not determined. In the ATENA series,[10] the overall morbidity was 2.3% and mortality 1.4% in the BRT group. The CLARITY series[8] reported findings similar to those of the ATENA, with treatment related morbidity as 2.5% and mortality as 1.3% in the remodeling group. Dabus et al, reported a 2.6% rate of procedure-related morbidity.[11] Limitations of this study are not recording the rates of procedure-related morbidity and mortality, the total balloon inflation time, the number of inflations per case, maximum single inflation time and reperfusion time between inflations. However, the average inflation time observed in this study was no more than 5 minutes. Spiotta et al,[21] in their balloon remodeling series for unruptured aneurysms reported no significant relationship between balloon inflation practices and incidence of ischemic complications.

Conclusion

The rates of adequate aneurysm occlusion and treatment related complications achieved in our aneurysm samples are similar to those reported in other studies on BRT. Majority of the ruptured and unruptured wide neck cerebral aneurysms can be successfully treated in our population with balloon remodeling technique for coil placement. This technique offers a safe and effective solution for endovascular treatment of wide neck and complex-origin cerebral aneurysms, where conventional non-assisted coil placement might not be possible.

Conflict of Interest: None to declare.

References

1. Layton KF, Cloft HJ, Gray LA, Lewis DA, Kallmes DF. Balloon-assisted coiling of intracranial aneurysms: Evaluation of local thrombus formation and symptomatic thromboembolic complications. Am J Neuroradiol. 2007;28(6):1172–5.
2. Moret J, Cognard C, Weill A, Castaings L, Rey A. The "Remodelling Technique" in the Treatment of Wide Neck Intracranial Aneurysms. Angiographic Results and Clinical Follow-up in 56 Cases. Interv Neuroradiol. 1997;3(1):21–35.
3. Piotin M, Blanc R. Balloons and stents in the endovascular treatment of cerebral aneurysms: Vascular anatomy remodeled. Frontiers in Neurology. 2014;5:1–9.
4. White AC, Khattar NK, Aljuboori ZS, Obiora JC, James RF. Basic endovascular techniques: Direct, balloon-assisted, and stent-assisted coil embolization. Intracranial Aneurysms. Elsevier Inc.; 2018. 329–56.
5. Cai K, Zhang Y, Shen L, Ni Y, Ji Q. Comparison of Stent-Assisted Coiling and Balloon-Assisted Coiling in the Treatment of Ruptured Wide-Necked Intracranial Aneurysms in the Acute Period. World Neurosurg. 2016; 96:316–21.
6. Wang F, Chen X, Wang Y, Bai P, Wang HZ, Sun T, et al. Stent-assisted coiling and balloon-assisted coiling in the management of intracranial aneurysms: A systematic review & meta-analysis. J Neurol Sci. 2016;364: 160–6.

7. Lazareska M, Aliji V, Stojovska-Jovanovska E, Businovska J, Mircevski V, Kostov M, et al. Endovascular treatment of wide neck aneurysms. Open Access Maced J Med Sci. 2018;6(12):2316–22.
8. Pierot L, Cognard C, Anxionnat R, Ricolfi F. Remodeling Technique for Endovascular Treatment of Ruptured Intracranial Aneurysms Had a Higher Rate of Adequate Postoperative Occlusion than Did Conventional Coil Embolization with Comparable Safety. Radiology. 2011;258(2):546–53.
9. Pierot L, Cognard C, Spelle L, Moret J. Safety and efficacy of balloon remodeling technique during endovascular treatment of intracranial aneurysms: critical review of the literature. AJNR Am J Neuroradiol. 2012; 33(1):12–5.
10. Pierot L, Spelle L, Vitry F. Immediate clinical outcome of patients harboring unruptured intracranial aneurysms treated by endovascular approach: Results of the ATENA study. Stroke. 2008;39(9):2497–504.
11. Dabus G, Brinjikji W, Amar AP, Almandoz JED, Diaz OM, Jabbour P, et al. Angiographic and clinical outcomes of balloon remodeling versus unassisted coil embolization in the ruptured aneurysm cohort of the GEL the NEC study. J Neurointerv Surg. 2018 May 1; 10(5):447–51.
12. Gory B, Rouchaud A, Saleme S, Dalmay F, Riva R, Caire F, et al. Endovascular treatment of middle cerebral artery aneurysms for 120 nonselected patients: A prospective cohort study. Am J Neuroradiol. 2014; 35(4): 715–20.
13. Chitale R, Chalouhi N, Theofanis T, Starke RM, Amenta P, Jabbour P, et al. Treatment of ruptured intracranial aneurysms: Comparison of stenting and balloon remodeling. Neurosurgery. 2013;72(6):953–9.
14. Pierot L, Barbe C, Nguyen HA, Herbreteau D, Gauvrit JY, Januel AC, et al. Intraoperative Complications of Endovascular Treatment of Intracranial Aneurysms with Coiling or Balloon-assisted Coiling in a Prospective Multicenter Cohort of 1088 Participants: Analysis of Recanalization after Endovascular Treatment of Intracranial Ane. Radiology. 2020;296(2):130–3.
15. Gentric JC, Biondi A, Piotin M, Mounayer C, Lobotesis K, Bonafé A, et al. Balloon remodeling may improve angiographic results of stent-assisted coiling of unruptured intracranial aneurysms. Neurosurgery. 2015; 76(4):441–5.
16. Bashir Q, Ahmed HN. Coil embolization of wide neck cerebral aneurysms using balloon remodeling technique-initial experience in pakistan. Pakistan J Neurol Sci. 2014;9(3).
17. Raymond J, Guilbert F, Weill A, Georganos SA, Juravsky L, Lambert A, et al. Long-term angiographic recurrences after selective endovascular treatment of aneurysms with detachable coils. Stroke. 2003; 34(6): 1398–403.
18. Consoli A, Vignoli C, Renieri L, Rosi A, Chiarotti I, Nappini S, et al. Assisted coiling of saccular wide-necked unruptured intracranial aneurysms: Stent versus balloon. J Neurointerv Surg. 2016;8(1):52–7.
19. Chalouhi N, Starke RM, Koltz MT, Jabbour PM, Tjoumakaris SI, Dumont AS, et al. Stent-assisted coiling versus balloon remodeling of wide-neck aneurysms: Comparison of angiographic outcomes. Am J Neuroradiol. 2013;34(10):1987–92.
20. Cottier JP, Pasco A, Gallas S, Gabrillargues J, Cognard C, Drouineau J, et al. Utility of balloon-assisted guglielmi detachable coiling in the treatment of 49 cerebral aneurysms: A retrospective, multicenter study. Am J Neuroradiol. 2001;22(2):345–51.
21. Spiotta AM, Bhalla T, Hussain MS, Sivapatham T, Batra A, Hui F, et al. An analysis of inflation times during balloon-assisted aneurysm coil embolization and ischemic complications. Stroke. 2011; 42(4): 1051 –5.

Authors Contribution

QB: Conceptualization of Project
QB, FF: Data Collection
QB, FF, JI: Literature Search
FF, AI: Statistical Analysis
QB, FF, AI, JI: Drafting, Revision
QB, FF, AI, JI: Writing of Manuscript

The Effect of Severity of Diabetes Mellitus on the Clinical Outcome of Patients Admitted with COVID-19 in a Tertiary Care Hospital

Nighat Jamal,[1] Salwa Anis,[2] Qazi Mohammad Waleed,[3] Hassan Mumtaz,[4] Syed Affan Ali,[5] Nimra Tul Ain[6]

Abstract

Objective: To determine the effect of the severity of diabetes mellitus on the outcome of diabetic people who had contracted the COVID-19 virus.

Method: This retrospective cross-sectional study was conducted from November 2020 to March 2021. 300 patients were confirmed cases of COVID-19 via RT-PCR. Demographic, clinical lab data, and outcome were collected and analyzed using SPSSv20.0 along with Chi Square.

Results: The average age of the participants was 56.95 12.856 years. Males made up the majority of our study's participants (60.7 percent). Diabetes (66.67%) was present in patients with moderate or mild disease (33.33%) and severe disease (33. 33%).Patients with mild to intermediate diabetes had an overall discharge rate of 80.8% and a death rate of 19.2%. Patients with severe diabetes were discharged at a rate of 58.7%, but 41.3% of them died as a result of their disease. 103 (66%) of the diabetics who had improved clinically maintained stable circumstances, compared to 53 (34%) of the diabetics who had stabilized.

Conclusion: In patients infected with COVID-19, uncontrolled hyperglycemia has a negative impact on the body's ability to fight infection. Patients with SARS-CoV-2 who are properly cared for and are taking appropriate medication may be able to keep their condition under control.

Keywords: diabetes mellitus, covid-19, mortality, hyperglycemia,

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Introduction

The new coronavirus, formerly known as the severe acute respiratory syndrome coronavirus-2, was given the designation "coronavirus disease 2019" (Covid-19) by the WHO in February of 2020. (SARS-Cov-2).[1] It was once thought that a unique coronavirus was to blame for an outbreak of pneumonia with an unknown source in China, but scientists found this on January 7, 2020. On March 11, 2020, the World Health Organization (WHO) proclaimed COVID-19 a pandemic.[2] The WHO reports that as of January 2, 2021, more than 82.5 million people had been infected by the COVID-19 virus, with 1,818,849 deaths. The number of confirmed cases in Pakistan was 482,178, with 10,176 deaths.[3]

Patients with COVID-19 exhibit a variety of symptoms, ranging from mild upper respiratory tract infections to severe pneumonia. Headaches, a loss of taste and smell, a fever, cough, body aches and shortness of breath are among the most common symptoms of COVID-19. Additionally, 5% of patients will experience a life-threatening condition characterized by multiple organ failure, respiratory failure, heart damage, and septic shock.[4] Covid 19's mortality and severity are influenced by a variety of circumstances. Many studies have shown a link between hypertension and the development of serious illness or mortality. Chronic renal disease, chro-

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nic pulmonary disease, diabetes, cerebrovascular accidents, and smoking have all been connected.[5] According to one study, more patients admitted to the ICU with known comorbidities were admitted to the ICU than those who were otherwise in perfect health.[6] Hypertension is the most common common co-morbidity among Covid-19 users, followed by diabetes. Generally, patients with diabetes are susceptible to more infections and hospital admissions, and a similar tendency has been reported in diabetics who have been infected with the COVID-19 virus.[7] Several studies have found that more than one-fifth of COVID-19 diabetics have severe or critical illness.[7] A patient with COVID-19 must have their blood sugar under control at all times. Studying SARS and influenza H1N1 has shown that poor glycemic control can lead to serious consequences and even death, but the data on COVID-19's blood glucose levels are scarce.[8] A study also showed that COVID-19 might increase the blood sugar levels of people whose blood sugar levels were otherwise within the usual limit.[9] Diabetes mellitus plays an important part in determining a patient's prognosis. It is imperative that this function be well understood in order to maintain a healthy blood sugar level. Patients infected with the COVID-19 virus had varied outcomes based on the severity of their disease.

Our aim was to determine the effect of the severity of diabetes mellitus on the outcome of diabetic people who had contracted the COVID-19 virus.

Methods

This retrospective cross-sectional study was conducted at a tertiary care hospital in Hazara Division. The total sample size collected was 300 patients during the time frame of November 2020 to March 2021. RT-PCR was used to confirm the cases of coronavirus infection. Ethical approval was taken from the concerned department of Ayub Teaching Hospital. Confirmed COVID-19 cases were included in the study. Those with suspected COVID-19 infection but no laboratory confirmation was excluded from the study. Demographic, clinical lab data, and outcome (survival or death) were collected from patient records and recorded on self-designed Performa. Data was analysed via SPSSv20.0. The Chi square test was used to assess the significance between the severity of diabetes mellitus and COVID-19 patients. Patients with blood glucose levels between 180 and 190mg/dl were classified as having mild COVID symptoms, while those with blood glucose levels above 200 mg/dl were classified as having moderate to severe disease. Data was analysed via SPSSv20.0. The Chi square test was used to assess the significance between the severity of diabetes mellitus and COVID-19 patients.

Results

The study had 300 participants with a mean age of 56.95 +/-12.856. Table I shows that the male gender predominated in our study (60.7%). Out of the 300 patients, 156 (52%) had diabetes mellitus, almost one-third of them (36.6%) had hypertension as a comorbidity, and the rest (15.7%) had a history of IHD. Table 1 further shows that out of 300 patients, almost two-thirds of them (69%) got discharged while around one-third (31%) got expired.

Table 1: *Patient Demographics & Co-morbid*

Variable		n (%)
Gender	Male	182 (60.7)
	Female	118 (39.3)
Diabetic	Yes	156 (52)
	No	144 (48)
Hypertensive	Yes	110 (36.6)
	No	190 (63.3)
IHD	Yes	47 (15.7)
	No	253 (84.3)
Clinical outcome	Discharged	207 (69)
	Expired	93 (31)

Table 2: *Severity of Diabetes Mellitus in association with its outcome*

Variable			Clinical outcome?		P value
			Discharged	Expired	
severity of diabetes	mild to moderate	Number (n)	42	10	0.010
		Percentage (%)	80.8%	19.2%	
	Severe	Number (n)	61	43	
		Percentage (%)	58.7%	41.3%	

Table 3: *Clinical Outcome in patients of Diabetes Mellitus*

Variable			Clinical outcome?		P value
			Discharged	Expired	
Do you have Diabete	Yes	Number (n)	103	53	1.344
		Percentage (%)	66.0%	34.0%	
	No	Number (n)	104	40	
		Percentage (%)	72.2%	27.8%	

Those patients who had diabetes were divided into two categories: those with moderate or mild disease (33.33%) and those with severe disease (66.67%), as shown in table II. The clinical outcome of those who had mild to moderate diabetes mellitus was such that the majority

(80.8%) of patients were discharged, and fewer (19.2%) patients expired. More than half (58.7%) of the patients who had severe diabetes mellitus were discharged, while 41.3% expired. The statistical association between the severity of diabetes mellitus and the outcome of the disease was significant with a p value of 0.010.

Discussion

In this study, fewer than a quarter (27.2%) of patients without diabetes died after being discharged from the hospital, while the majority (72.2 percent) were in stable health. We discovered that more individuals with severe diabetes than those who had mild to moderate diabetes died, we discovered. Patients with mild to moderate diabetes, as opposed to those with severe diabetes, were discharged in greater numbers. As can be shown, diabetes severity has a significant impact on how well diabetics fare after contracting the COVID-19 virus.

There has been no other study to date that looked at the relationship between diabetes severity and clinical outcomes of the COVID-19. Therefore, ours is unique. However, our findings are in line with those of other research that has looked at this population. In a study by Fadini et al., patients with a mean blood glucose level of 192.6 88.2 mg/dl (a mild to moderate form of diabetes) were more likely to be discharged alive (56.1 percent) than to be dead. According to the same research, more patients (78.8%) with no diabetes were discharged than were euthanized.[10]

According to Bode B et al., severely diabetic patients (71.2 percent) were more likely to be released from the hospital alive than dead, with a mean blood glucose level of 115.6 mg/dl (28.8 percent), according to Bode B et al. The number of patients with no diabetes who were released alive was high (93.8 percent), while the number of patients who died was lower (6.2 percent), just as we found in our study.[11]

Diabetes and hyperglycemia cause a disorder known as "diabetic lung," which results in decreased lung capacity. Patients with hyperglycemia have a worse prognosis because of abnormalities in the lungs.[13] Coagulopathies and systemic inflammation caused by hyperglycemic pulmonary microangiopathy,[14–15] have been established as common risk factors for diabetic lung. Because Covid-19 causes systemic inflammation and coagulopathy, it stands to reason that hyperglycemia and Covid-19 clinical outcomes are linked.[17] Research from the United Arab Emirates demonstrates that uncontrolled hyperglycemia has a negative impact on COVID-19 patients. Complications are more likely in cases of newly diagnosed or previously undetected hyperglycemia. For patients in the hospital, optimising glycemia and screening for undetected diabetes may be particularly essential in the context of the COVID-19 pandemic.[17] The same may be said for an early pandemic study conducted in north India, which came to the same conclusion. Comorbidities such as diabetes, hypertension, cardiovascular disease (CAD), chronic kidney disease (CKD), and cancer are substantially associated with death in the COVID-19 infection. These patients' clinical results can be improved by early triaging and intensive treatment.[18]

There were many changes in the clinical profile of the COVID-19 patients in Karachi during their hospital stay, which affected their prognosis, according to a case series analysis. Tocilizumab, remdesivir, doxycycline, ivermectin, enoxaparin sodium, and steroids have been identified as prospective therapeutic alternatives for COV ID-19 because of their ability to alter disease severity and recovery rate.[19]

In elderly patients who already have serious and critical infections, COVID-19 infection is an even more serious concern. In diabetics, immunoresponse abnormalities play a crucial part in escalating the disease's severity. Diabetic patients may be more susceptible to COVI-19 if they have obesity, cardiovascular disease, and hypertension. [20]

Conclusion

In patients infected with COVID-19, uncontrolled hyperglycemia has a negative impact. Glycemic control in hospitalized patients is critical. Patients with SARS-CoV-2 who are properly cared for and are taking appropriate medication may be able to keep their condition under control.

Conflict of Interest *None*

References

1. Zhou F, Yu T, Du R, Fan G, Liu Y, Et Al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan. Lancet Infect Dis. 2020; 395 (10229): 1054-1062.
2. Noor, F.M., Islam, M.M. Prevalence and Associated Risk Factors of Mortality Among COVID-19 Patients: A Meta-Analysis. J Community Health 45, 1270– 1282 (2020).

3. Coronavirus disease (COVID-19) Weekly Epidemiological Update and Weekly Operational Update. Coronavirus Disease (COVID-19) Situation Reports (who.int)
4. Hassan S, Sheikh F N, Jamal S, et al. Coronavirus (COVID-19): A Review of Clinical Features, Diagnosis, and Treatment. Cureus 12(3) 2020.
5. Williamson, E.J., Walker, A.J., Bhaskaran, K. et al. Factors associated with COVID-19-related death using OpenSAFELY. Nature 584, 430–436 (2020).
6. Yang J, Zheng Y, Gou X, Pu K, Chen Z, Guo Q, et al. Prevalence of comorbidities and its effects in patients infected with SARS-CoV-2: a systematic review and meta-analysis. Int J Infect Dis. 2020 May;94:91-95
7. John M. Dennis, Bilal A Mateen, Raphael Sonabend , Nicholas J. Thomas, et al. Type 2 Diabetes and COVID-19– Related Mortality in the Critical Care Setting: A National Cohort Study in England, March–July 2020. Diabetes Care 2021 Jan; 44(1): 50-57
8. Singh AK, Gupta R, Ghosh A, Misra A. Diabetes in COVID-19: Prevalence, pathophysiology, prognosis and practical considerations. Diabetes Metab Syndr. 2020;14(4):303-310.
9. Lim S, Bae JH, Kwon H, et al. COVID-19 and Diabetes Mellitus: From Pathophysiology to Clinical Management Nature Reviews Endocrinology, 2021, vol 17, 11-30. https://doi.org/10.1038/s41574-020-00435-4
10. Fadini GP, Morieri ML, Boscari F, Fioretto P, Maran A, Busetto L, et al. Newly-diagnosed diabetes and admission hyperglycemia predict COVID-19 severity by aggravating respiratory deterioration. Diabetes Res Clin Pract.2020 Oct;168:108374. doi:10.1016/ j.diabres. 2020.108374. Epub 2020 Aug 15. PMID: 32805345; PMCID: PMC7428425.
11. Bode B, Garrett V, Messler J, McFarland R, Crowe J, Booth R, Klonoff DC. Glycemic Characteristics and Clinical Outcomes of COVID-19 Patients Hospitalized in the United States. J Diabetes Sci Technol. 2020 Jul; 14(4):813-821. doi: 10.1177/1932296820924469. Epub 2020 May 9. Erratum in: J Diabetes Sci Technol. 2020 Jun 10;: 1932296820932678. PMID: 32389027; PMCID: PMC7673150.
12. Fuso L., Pitocco D., Antonelli-Incalzi R. Diabetic lung, an underrated complication from restrictive functional pattern to pulmonary hypertension. Diabetes Metab Res Rev. 2019;35
13. Caruso I, Giorgino F. The diabetic lung: An easy target for SARS-CoV-2? Diabetes Metab Res Rev. 2020 Nov; 36(8):e3346. doi: 10.1002/dmrr.3346. Epub 2020 Jun 18. PMID: 32426928; PMCID: PMC7267106.
14. Tiengo A., Fadini G.P., Avogaro A. The metabolic syndrome, diabetes and lung dysfunction. Diabetes Metab. 2008;34:447–454.
15. Jagadapillai R, Rane MJ, Lin X, Roberts AM, Hoyle GW, Cai L. Diabetic microvascular disease and pulmonary fibrosis: the contribution of platelets and systemic inflammation. Int J Mol Sci. 2016 Vol. 17, no. 11 p. 1853. https://doi.org/10.3390/ijms17111853
16. Jose RJ, Manuel A. COVID-19 cytokine storm: the interplay between inflammation and coagulation. Lancet Respir Med. 2020 Jun; 8(6): e46-e47. doi: 10. 1016/S2213-2600(20)30216-2.
17. Hafidh K, Abbas S, Khan A, Kazmi T, Nazir Z, Aldaham T: The Clinical Characteristics and Outcomes of COVID-19 Infections in Patients with Diabetes at a Tertiary Care Center in the UAE. Dubai Diabetes Endocrinol J 2020;26:158-163. doi: 10.1159/000512232
18. Kantroo V, Kanwar MS, Goyal P, Rosha D, Modi N, Bansal A, et al. Mortality and Clinical Outcomes among Patients with COVID-19 and Diabetes. Med. Sci. 2021, 9, 65. https://doi.org/10.3390/ medsci9040065
19. Ahsan T, Rani B, Siddiqui R, et al. (April 29, 2021) Clinical Variants, Characteristics, and Outcomes Among COVID-19 Patients: A Case Series Analysis at a Tertiary Care Hospital in Karachi, Pakistan. Cureus 13(4): e 14 761. doi:10.7759/cureus.14761
20. Verma AK, Beg MMA, Bhatt D, Dev K, Alsahli MA, Rahmani AH, Goyal Y. Assessment and Management of Diabetic Patients During the COVID-19 Pandemic. Diabetes Metab Syndr Obes. 2021;14:3131-3146

Authors Contribution

NJ: Conceptualization of Project
QMW: Data Collection
NTA : Literature Search
SAA, HM: Drafting, Revision
SA: Writing of Manuscript

Comparative Analysis of Oxytocin Versus Vaginal Prostaglandin in Induction of Labour in Pre Labour Rupture of Membrane

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Abstract

Objective: To determine the mean time from induction to delivery after spontaneous pre-labour rupture of membrane using I/V oxytocin versus vaginal prostaglandin E2.

Method: The study was randomized clinical trial carried out in gynae unit IV Sheikh Zayyed Hospital Lahore. Over a period of six months from July 2019 to Dec 2019. A total of 100 pregnant ladies with age range 18 years to 40 years and having gestational age > 37 weeks were included. Pregnant women with twin pregnancy, and with placenta previa or abruptio placenta and females with any known fetal or maternal risk assessed on clinical examination and those who have congenital abnormality at the time of presentation were also excluded from study. Later on patients were divided randomly into two groups using random number table. Group A (50 patients) patients was given intravenous oxytocin 1 m unit/min in infusion while group B (50 patients) patients was given 3mg prostaglandin E2 vaginaly. Effect modifier like BMI, hypertension and pregnancy induced hypertension will also be recorded. Patients were observed for the time of induction of delivery as per operational definition. Data was entered on computer software SPSS version 21 Independent t-test was applied to compare the mean time between both groups.

Results: There was significant difference between two groups for mean duration of labor as mean duration of induction of labor was 3.92±1.74 in the oxytocin group while 9.38±3.71 in prostaglandin group with a p-value of 0.001.

Conclusion: Oxytocin is effective in terms of reduction in time of induction of labor to delivery as compared to prostaglandin E2.

Keywords: oxytocin, prostaglandin, pre-rupture of membrane

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Introduction

Labour is defined as regular painful uterine contractions with progressive cervical effacement & dilatation accompanied by descent of presenting part resulting in expulsion of fetus from the uterus.[1] Premature rupture of membranes (PROM), is rupture of the membranes before start of labour, It affects 5-10% among all pregnancies, and 60% of the time it happens before the baby is born.[2] Labour begins spontaneously within 24 hours of membranes ruptures. With hoping conservative management, about 60.0-80.0% of PROM patients will go into spontaneous labour within 24 hours of the rupture of membranes, and approximately 95% within 72 hours. But 4% of such patients will not experience spontaneous labour till seven days even. In spite of many studies available in the literature, the clinical management is surprisingly still controversial.[3] If the time between leakage and birth is longer than 18 hours, the risk of infant infection and hospitalization increases.

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Reported incidence of neonatal sepsis is 2.0-4.0%.[3] Fetal hypoxia can occur due to cord prolapse, cord compression and abruption of placentae. Other risks include, sub-clinical chorioamnionitis, increased likelihood of operative delivery, increased incidence of marginal cord insertion which itself is associated with retained placenta & both primary and secondary postpartum hemorrhage. Management of PROM involves a balance between expectant management and intervention.[4]

However, induction of labour compared with expectant management only, reduces the risk of maternal and neonatal complications. Various mediators that stimulate uterine contractions & cervical ripening have been introduced, but only a few have been evaluated scientifically. For inducing labour, intravenous Oxytocin and other prostaglandin formulations have been utilised, but their success varies.[5] If rupture of membranes occurs at term between 37 and 41 weeks of gestation at this time it is referred as pre-labor rupture of membranes.[6]

Although the approach of expectant management may appear to be warranted at first, postnatal problems have been found in 17% of expectantly managed patients. Infections are among the neonatal risks of expectant treatment (2.8 percent), admission to ICU (8.0%) and placental abruption, fetal pain (2.0%), deformities caused by foetal restriction. The most commonly used pharmaceutical drug is oxytocin.[7]

Induction is specify when there is a risk of pregnancy continuing, for the sake of the mother or fetus, exceeds the associated risk with induced labour & delivery. The sign has to be convincing, compelling and well documented. In order to acquire clear permission, the cause for induction and the techniques should also be discussed between the medical provider and the lady. When induction is offered simply for the convenience of the medical provider or the patient, these requirements are not met.[8] While in another study the time for induction of labor to birth was >5.0hrs smaller in the amniotomy group (24.7 / 30.0 hrs; average difference, 5.12 h; 95% CI, –2.50 to –7.79). Less women in the amniotomy group remained undelivered after 24 hours (47.2% / 67.6%; P < .01).9 The rationale of the study is to reach on a consensus regarding the effectiveness of oxytocin and prostagaldin for time of induction to delivery in women who have rupture of membrane before labour. This need arises due to controversy among the literature published internationally.[6,10] Moreover in an another study[8] it has not mentioned the standard deviation with mean time so the results are not clear. The results of this study will help us to measure the actual time of delivery from induction.

Material and Methods

This randomized Clinical Trial was conducted from July 2019 to December2019 in the Gynaecology department of Ethical approval was taken from Institutional Board of the hospital. Written consent was obtained from patients. The sample size 100 cases were calculated with 95% confidence level, 80% power of study taking an expected mean time between induction to delivery in the oxytocin group as 3.4±1.5 and in prostaglandin group as 9.6±4.7 hours.10 Patients of age 18-40 years having singleton pregnancy on ultrasonography with gestational age >37weeks. Females also presenting with PROM was expectantly managed for first 6 hours from the onset of ROM were also included from the study. Females with any known fetal or maternal risk assessed on clinical examination and those who have congenital abnormality at the time of presentation. Pregnant ladies with twin and triplet pregnancy. Those with gestational age less than 37 weeks. With placenta pravia and abruption placenta. Patients were interviewed for their demographics variables like age, gestational age, name and contact details. Later on patients were divided randomly into two groups using random number table. Group A (50 patients) patients was given intravenous oxytocin 1 munit/min intravenous (infusion diluted in normal saline) while group B (50 patients) patients was given 3mg prostaglandin vaginally once and labor was monitored with electronic fetal heart monitoring via CTG machine along with tocometer for assessing uterine contractions and cervical dilatation monitored using bishop scoring. Effect modifier like BMI, hypertension and pregnancy induced hypertension were recorded. Patients were observed for the time of induction of delivery as per operational definition. All data was collected through predesigned proforma attached. Data was entered in SPSS-21. Quantitative variables like age, BMI, gestational age and mean time from induction to delivery in both groups was presented as mean ± SD. Independent t-test was applied to compare the mean time between both groups. Data was stratified for the variables i.e. age, gestational age, hypertension, PIH and BMI. Post-stratification independent t-test was applied to check the significance with P value ≤ 0.05 as significant.

Results

In this study, total 100 patients were included the mean age of the women was 33.28±7.61 years. Majority of the female were having a parity of 4 with frequency of 30 (30%)(Table-2). Mean gestational age of the patients was 38.87±1.14 weeks. Mean duration of induction of labor was 6.65±3.97 hours. Number of Parity as shown in (Table-1). Pregnancy induced hypertension was fond in 27 cases (27%) as 73(73%) were free from this condition. (Table-2) There was significant difference for mean duration of labor as mean duration of induction of labor was 3.92±1.74 in the oxytocin group while 9.38±3.71 in prostaglandin group with a p-value of 0.001 (Table-3). When data was stratified, it was note that there was significant difference with respect other factors. Mean duration of induction of labor was 3.31± 1.88 in oxytocin and 10.61±3.89 in prostaglandin who were in age group of 18-30 years and this was significant difference. Similarly, there was significant difference for the gestational age, hypertension and pregnancy induced hypertension in the both treatment groups with a less than p-value 0.05 as considered in (Table-4).

Table 1: *Distribution of Age and Gender*

Age	Mean ±SD
Mean	33.82± 7.61
Gestational Age	38.87± 1.14
Mean duration from induction to labor	6.65 ±3.97
Parity	
1	9(9.0%)
2	21(21%)
3	11(11.0%)
4	30(30%)
5	17(17%)
6	12(12%)

Table 2: *Distribution of Hypertension*

		Frequency (%)
Hypertension	Yes	30(30%)
	No	70(70%)
Pregnancy induced hypertension	Yes	27(27%)
	No	73(73%)

Table 3: *Comparison of Mean Time of Induction of Labor in both Treatment Groups*

Duration of induction of labour	Mean ± SD	P value
Oxytocin	3.92±1.72	**0.001**
Prostaglandin	9.38±3.71	

Table 4: *Stratification with respect to Age, Gestational age for the mean duration of induction labor.*

		Oxytocin Mean± SD	Prostagladin Mean± SD
Age Group	18-30 years	3.31± 1.88	10.61± 3.89
	>30 years	4.20± 1.59	8.48± 3/36
	P value	**0.001**	**0.02**
Gestational Age	37-39 weeks	4.03± 1.66	9.82± 3.70
	>39weeks	3.70± 1.86	8.43± 3.66
	P value	**0.001**	**0.00**
Hypertension	Yes	3.66±1.67	10.33±4.41
	No	4.02±1.75	8.97±3.35
		0.000	0.000
PIH	Yes	4.00±1.41	9.62±3.77
	No	3.89±1.81	9.26±3.73
	P value	0.001	0.0001

Discussion

All pregnancies would be carried to term in such an ideal world, and labour would commence spontaneously. In fact, it's generally preferable to deliver the baby before natural labour starts. When deciding whether to conduct a caesarean section or induce labour for a vaginal delivery, the physician considers the mother's & fetus medical stability.[11] The stimulation of uterine contractions to achieve delivery before the commencement of natural labour is known as labour induction. Since the 1950s, when oxytocin (Pitocin) was synthesized, this method has been widely used; In the United States, approximately 13% of live births are currently induced. The majority of labour inductions are performed for postdate pregnancies, which account for around 10% of all live deliveries.12By 32 weeks of pregnancy, oxytocin receptor in the uterus have increased 100-fold, and by parturition, they have increased 300-fold. Although significant for the actual labour process, higher oxytocin sensitivity only predicts the duration of labour to a little extent, as parity and cervical state at the time of labour are more important factors. In the United States, oxytocin is one of the most regularly utilized medications. While individual patients differ in oxytocin sensitivity and reaction, the pathophysiology of oxytocin-stimulated labour is comparable to that of spontaneous labour. According to synthetic oxytocin pharmacokinetic studies, uterine response occurs after 3–5 minutes of infusion, and a stable level of oxytocin in plasma is reached after 40 minutes.[13] Uterine response to oxytocin is determined by the length of pregnancy.

From 20 to 30 weeks of pregnancy, there is a progressive increase in response, From 34 weeks of pregnancy until term, there is a plateau, after which sensitivity increases. Lower BMI, higher cervical dilatation, parity, or gestational age are all predictors of a good oxytocin induction response.[14] In a study The oxytocin/PGE2 group consisted of 112 patients who experienced PGE2 cervical instillation 6.0 h already continuous oxytocin infusion. Induction to the active phase of labour was successful in 96 women (85.69%) in the misoprostol group versus 86.0 women (76.8%) in the oxytocin/PGE2 group, however the misoprostol group (9.2+2.4 h) had a considerably shorter medication initiation delivery interval than the oxytocin/PGE2 group (15.2+3.2 h, P value :0.001)[15] which was similar as the results noted in this study but the time of induction in prostaglandin group was different in our study.

Conclusion

Intravenous Oxytocin is more effective in induction of labour in Pre Labour Rupture of Membrane as compared to vaginal prostaglandins.

Conflict of Interest None

References

1. Muhunthan K. Pelvic fetal cranial Anatomy and the stages and mechanism of labor. Best Practice in Labour and Delivery. 2016:1.
2. Rodrigo MRR, Kannamani A. Perinatal and maternal outcome in premature rupture of membranes. Proteus. 2016;2:13-33.
3. Obstetricians ACo, Gynecologists. Practice bulletin no 160: Premature rupture of membranes. Obstetrics & Gynecology. 2016;127(1):e39-e51.
4. Menon R, Moore JJ. Fetal membranes, not a mere appendage of the placenta, but a critical part of the fetal-maternal interface controlling parturition. Obstetrics and Gynecology Clinics. 2020;47(1):147-62.
5. Ferguson KK, McElrath TF, Chen Y-H, Loch-Caruso R, Mukherjee B, Meeker JD. Repeated measures of urinary oxidative stress biomarkers during pregnancy and preterm birth. American journal of obstetrics and gynecology. 2015;212(2):208. e1-. e8.
6. Kruit H, Tolvanen J, Eriksson J, Place K, Nupponen I, Rahkonen L. Balloon catheter use for cervical ripening in women with term pre-labor rupture of membranes: A 5-year cohort study. Acta obstetricia et gynecologica Scandinavica. 2020;99(9):1174-80.
7. Aagaard-Tillery KM, Nuthalapaty FS, Ramsey PS, Ramin KD. Preterm premature rupture of membranes: perspectives surrounding controversies in management. American journal of perinatology. 2005;22(06):287-97.
8. Echebiri NC, McDoom MM, Pullen JA, Aalto MM, Patel NN, Doyle NM. Placental alpha-microglobulin-1 and combined traditional diagnostic test: a cost-benefit analysis. American journal of obstetrics and gynecology. 2015;212(1):77. e1-. e10.
9. Beckmann M, Kumar S, Flenady V, Harker E. Prostaglandin vaginal gel induction of labor comparing amniotomy with repeat prostaglandin gel. American journal of obstetrics and gynecology. 2015;213(6):859. e1-. e9.
10. Longini M, Perrone S, Vezzosi P, Marzocchi B, Kenanidis A, Centini G, et al. Association between oxidative stress in pregnancy and preterm premature rupture of membranes. Clinical biochemistry. 2007; 40(11) :793-7.
11. Cunningham F, Leveno K, Bloom S, Spong CY, Dashe J. Williams obstetrics, 24e: Mcgraw-hill New York, NY, USA; 2014.
12. Frey HA, Tuuli MG, England SK, Roehl KA, Odibo AO, Macones GA, et al. Factors associated with higher oxytocin requirements in labor. The Journal of Maternal-Fetal & Neonatal Medicine. 2015;28(13):1614-9.
13. Thamer H. Assessment of Nurses' Knowledge regarding oxytocin administration during Labor at maternity hospitals in Al-Kut City. Iraqi National Journal of Nursing Specialties. 2014;1(27):1-10.
14. Bahadori F, Ayatollahi H, Naghavi-Behzad M, Khalkhali H, Naseri Z. Predicting factors on cervical ripening and response to induction in women pregnant over 37 weeks. Medical ultrasonography. 2013;15(3):191-8.
15. Kadanali S, Küçüközkan T, Zor N, Kumtepe Y. Comparison of labor induction with misoprostol vs. oxytocin/prostaglandin E2 in term pregnancy. International Journal of Gynecology & Obstetrics. 1996;55(2):99-104

Authors Contribution

SD: Conceptualization of Project
WN: Data Collection
AJ : Literature Search
RS: Statistical Analysis
RS: Drafting, Revision
MM: Writing of Manuscript

Original Article

Association of Depression, Anxiety, and Musculoskeletal Symptoms with Internet Addiction Amongst Undergraduates of University

Noor-ul-Ain Waheed,[1] Mushayyada Rathore,[2] Amna Ihsan,[3] Irsa Asif,[4] Rijha Ahmed,[5] Khaulah Qureshi [6]

Abstract

Objective: To find association of depression, anxiety, and musculoskeletal symptoms with internet addiction amongst undergraduates of King Edward Medical University during Covid-19 induced lockdown.

Method: This was a Cross-sectional analytical study, conducted in Biochemistry Department of KEMU, Lahore from October to December 2020. A total of 400 undergraduate students enrolled in various programs of the university, Lahore fulfilling selection criteria were included in the study. Data were recorded using Google doc. Patient Health Questionnaire-2, Generalized Anxiety Disorder-2, and Modified version of Nordic Musculoskeletal Questionnaire were used to detect clinically significant depression, anxiety, and to record musculoskeletal symptoms respectively. The participants were classified into three categories namely low, moderate, and severe level of internet addiction based on Young's Internet Addiction Test score.

Results: The mean age of study subjects was 20.5 ± 1.5 years. Most of them were females (n=253, 63.3%), and of MBBS degree program (n=268, 67%). Majority showed moderate level of internet addiction (n=287, 71.8%). Amongst those who had severe level of internet addiction, more (17%) were found to have anxiety as compared to those who did not have it (6.8%). Similarly, more number (17.7%) was observed in depression category than no depression category (5.9%). Likewise, comparing presence of musculoskeletal symptoms with level of internet addiction, significant association was established ($p<0.001$).

Conclusion: Various levels of internet addiction amongst participants showed significant association with anxiety, depression, and musculoskeletal symptoms during covid-19 induced lock down.

Keywords: internet addiction, patient health questionnaire, generalized anxiety disorder, internet usage, undergraduate, medical students, covid-19

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Introduction

The biological response of human body to psychological stress is very similar to the biological response induced by physical diseases or microbial infections. Today, we have evolved to a computationally smart lifestyle, where we utilize screens frequently in our daily lives. Screen could be a television set, a computer terminal, or a handheld electronic device, such as a tablet or a smartphone. Cognitive stimulation by these electronic devices can cause a cascade of neurophysiological interactions like stress, which can have a significant impact on the brain's information processing capacity.[1] Stress adaption is a process in which people cope with stress by using a combination of various coping strategies. The increased use of electronic media is leading towards some new media-based stress manage-

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ment strategies. Modern electronic devices are the most used items for entertainment, which can help with avoidance-coping by offering a diversion from the stressor.[1,2]

Covid-19 pandemic has led towards financial, mental, and physical health problems which are the major stressful events globally. Changes in daily routine of life (decreased physical activity and loneliness) together with imposed stress are responsible for excessive use of electronic devices during this pandemic. University students are no exception to this as lockdown had forced them to depend on internet not only for entertainment and communication but also for education purposes because they are continuing their education through e-learning.[3]

Because modern screens are interactive, they increase the risk of their excessive use to access the internet, perhaps leading to internet addiction. "Internet addiction" also known as "compulsive internet usage," and "problematic internet use," is an impulsive shift in human behavior in which a person loses control over his or her use of the internet.[4]

Internet dependency has various adverse effects on mental and physical health such as increased risk of depression, anxiety, and musculoskeletal problems.[5] Frequent use of electronic devices with incorrect posture also aggravate musculoskeletal problems resulting in pain, mobility restrictions, and decreased functional ability and most people with musculoskeletal problems suffer with back, neck, and shoulder pain.[6]

To our knowledge, limited data is available in which impact of Covid-19 induced lockdown on internet dependency and its effect on mental and physical health are explored, especially in youngsters.

Material and Methods

This cross-sectional analytical study was conducted at Biochemistry Department of KEMU, Lahore from October to December 2020 after obtaining ethical approval from Institutional Review Board of KEMU vide letter no.726/RC/KEMU dated:10/10/2020. We included both male & female undergraduate students of age 18-25 years, studying in all academic years of various ongoing programs of KEMU including MBBS, DPT, and Allied Vision and Health Sciences after getting their consent to participate in the study. Only those undergraduate students at the university, who had Wi-Fi facility or internet connection during Covid-19 induced lockdown period took part in the study. The undergraduate students studying in the university who faced long hours' power shut down and provided with poor internet signal strength were excluded from our study. Sample size of 400 students was calculated taking a confidence level of 95%, absolute precision of 5% with expected prevalence of depression amongst students as 60%.[1] Responses of study subjects were recorded using Google doc-based questionnaire. Weblink of the questionnaire was first shared with class representatives of each program through WhatsApp messenger and subsequently it was shared with other students of the respective classes. Hence, data were collected through snowball sampling technique and confidentiality of study participants was also ensured. Questionnaire used in the study consisted of 31 closed ended questions to ask about background characteristics, to assess anxiety, depression & internet addiction and to record musculoskeletal symptoms (MSS) and mode of learning as e-learning amongst study subjects. Patient Health Questionnaire-2 (PHQ-2) and Generalized Anxiety Disorder-2 (GAD-2) are valid & reliable brief screeners which were used to detect clinically significant depression and anxiety[7] respectively. Therefore, presence & severity of internet addiction was determined by using Young's IAT.[4] Modified version of Nordic Musculoskeletal Questionnaire (mNMQ) was used to record MSS including pain & discomfort in 9 body regions amongst participants of the study.[5,8] A few questions were also asked to record their responses to observe effect of confounders on anxiety, depression, and MSS. These confounding variables included Covid-19 illness of study participants or of their family members or friends, loss of loved one due to Covid-19, financial crisis, academic delay, fear of professional examination, and fear of getting covid-19 infection.

Scores obtained from questions asked using GAD-2 & PHQ-2 on a 5-point Likert type scale ranged from 0-6 with a cut-off score of ≥3 to find clinically significant anxiety and depression,[7] respectively amongst study respondents. Regarding level of internet addiction, participants were classified into three categories based on IAT score. Those who scored 0-19, 20-39, 40-69, and 70-100 were considered as having no addiction, low level, moderate level, and severe level of internet addiction respectively.[4]

Recorded data of subjects of our study included age, gender, degree program, academic year, Body Mass Index, history of Covid-19 illness, IT device used for internet, purpose of use of IT device, use of IT device with proper posture, e-learning time spent per day, opi-

nion regarding e-learning is better than traditional learning, and sources used for e-learning. Data of study participants were analyzed using SPSS version 23. Descriptive statistics of quantitative variables such as age & BMI were calculated through mean ± SD and of the remaining qualitative variables through determining their frequencies & percentages. Levels of internet addiction among study respondents were also cross tabulated with anxiety, depression, musculoskeletal pain/discomfort during internet use, duration of trouble due to musculoskeletal symptom, use of internet without taking break, and daily duration of leisure activity on internet. Chi-square test was applied to determine association among qualitative variables and p-value was considered significant if it was less than 0.05.

Results

In our study, a total of 400 undergraduate students were included as participants whose mean age was 20.5 ± 1.5 years. Most of them were females (n=253, 63.3%), and of MBBS degree programme (n=268, 67%). Among study respondents, majority were studying in second year of their respective degree programme (n=158, 39.5%) and had normal BMI (n=249, 62.3%). Moderate level of internet addiction was observed in most of the students (n=287, 71.8%) whereas anxiety, depression, and musculoskeletal symptoms were recorded in 48.5%, 49.3%, and 52.8% of the study subjects respectively. Only 55 students (13.8%) had history of Covid-19 illness. During Covid-19 induced lockdown, majority of the study subjects used smartphone (n=338, 84.5%) as IT device. IT devices were used mostly for social networking system including WhatsApp & Facebook followed by entertainment purpose (n=135, 33.8%). Many of the respondents of the study rarely (n=159, 39.8%) and never (n=128, 32%) used IT device with proper posture. On asking about musculoskeletal symptoms in body regions, participants were observed as having high frequency of these symptoms in neck (n=166,41.5%) followed by back (n=131, 32.8%) amongst other body regions. Only 52 students (13%) used IT device mostly for the sake of e-learning and majority of the students consumed only 1-2 hours (n=107,26.8%) followed by 2-3 hours (n=94, 23.5%) daily on e-learning. When asked about their opinion regarding e-learning vs traditional learning, 60% of students disagreed that e-learning is better than traditional learning whereas only 17% of them agreed to this statement. The most used e-learning sources amongst our study participants were Google Classroom and Youtube (n=280, 70%). (Table-1)

When different levels of internet addiction were compared with various degree programs of study subjects, no significant difference was observed (p-value= 0.351) as shown by percent bar graph (Fig-1)

Fig-1: *100% component bar chart showing frequencies of participants with different levels of internet addiction against various degree programs at KEMU(N=400), p-value= 0.351, χ2 =4.43, df=4.*

Similarly, no significant difference was found when our study participants' daily duration of leisure activity on internet was compared amongst various degree programs (p-value=0.213), considering degree program as confounding variable. This is shown in bar graph as (Fig-2).

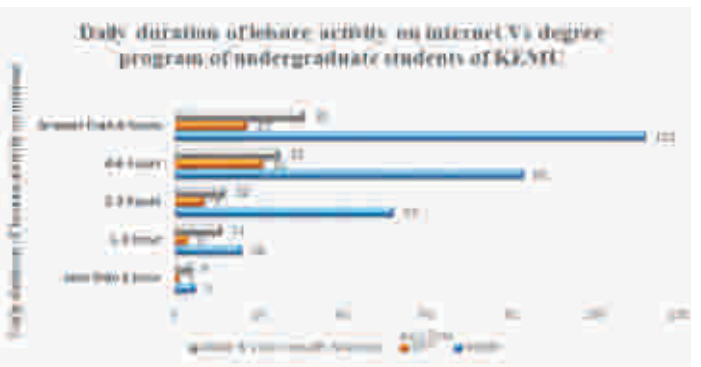

Fig-2: *Frequency of study participants of various degree programs at KEMU spending time on internet for leisure activity (N=400) p-value= 0.213, χ2 =10.8, df=8*

Fig-3: *Duration of internet usage by study subjects without taking break in different levels of internet addiction (p-value <0.001, χ2 =19.1, df=4)*

When duration of internet usage without taking break by the respondents was plotted against different levels of internet addiction, it was noted that highest percentage of respondents who used internet for >5 hours without any break were having severe level of internet addiction. Moreover, significant difference was revealed with p-

Table 1: *Background characteristics of undergraduate students of KEMU as study participants*

Variables	n (%)	Variables	n (%)
Age in years	20.5 ±1.5 (mean ± SD)	**Use smartphone/laptop with proper posture**	
		Never	128 (32%)
Gender		Rarely	159 (39.8%)
Male	147 (36.8%)	Occasionally	79 (19.8%)
Female	253 (63.3%)	Frequently	31 (7.8%)
		Always	3 (0.8%)
Degree Program		**IT devices used**	
MBBS	268 (67%)	Smartphone	338(84.5%)
DPT	49(12.3%)	TV	14 (3.5%)
Vision & Allied	83(20.8%)	Computer	4 (1%)
Health Sciences		Laptop	38 (9.5%)
		Tablet	6 (1.5%)
Academic Year		**Musculoskeletal symptoms in body regions**	Of total study participants n=400
First	117 (29.3%)	Neck	
Second	158 (39.5%)	Shoulders	166 (41.5%),
Third	39 (9.8%)	Hands/wrists	97 (24.3%)
Fourth	56 (14.0%)	Back	83 (20.8%)
Final	30 (7.5%)	Hips/thighs	131 (32.8%)
			30 (7.5%)
Body Mass Index (BMI)	22.1 ± 4.07 (mean ± SD)	**Daily duration of e-learning**	
		< 30 minutes	67 (16.8%)
BMI Categories		30-60 minutes	90 (22.5%)
Underweight	69 (17.3%)	1-2 hour	107 (26.8%)
Normal	249 (62.3%)	2-3 hours	94 (23.5%)
Overweight	67 (16.8%)	4-6 hours	29 (7.3%)
Obese	15 (3.8%)	> 6 hours	13 (3.3%)
Levels of internet addiction based on YIAT score		**Purpose of use of IT devices**	
		Social networking system (WhatsApp, Facebook)	167 (41.8 %)
low level	66 (16.5%)	Education	52 (13 %)
moderate level	287 (71.8%)	Communication (Calls, SMS)	9 (2.3 %)
severe level	47 (11.8%)	Gaming	22 (5.5 %)
Depression		Entertainment (Movie, Music)	135 (33.8 %)
Anxiety	197(49.3%)	Web surfing	12 (3%)
Complaint of Musculoskeletal	194 (48.5%)	Online shopping	3 (0.8%)
symptoms	211(52.8%)		
History of Covid 19 illness	55(13.8 %)	**e-learning sources used**	
e-learning is better than traditional learning		Google Classroom	156 (39%)
		YouTube	124 (31%)
Strongly Disagree	127 (31.8%)	Zoom	66 (16.5%)
Disagree	114 (28.5%)	Google search	22 (5.5%)
Neutral (both are same)	90 (22.5%)	Wikipedia	5 (1.3%)
Agree	47 (11.8%)	PowerPoint slides	11 (2.8%)
Strongly Agree	22 (5.5%)	Video lectures	3 (0.8%)
		E-Books	6 (1.5%)
		Netflix	5 (1.3%)
		All above mentioned sources	2 (0.5%)

value <0.001, $\chi 2$ =95.41, df=12 (Fig-3)

When responses of our participants with musculoskeletal symptoms during IT device usage were recorded on Likert scale, majority of the respondents who never & rarely (n=169/287, 59%) maintained their proper posture using IT device, were having MS symptoms and the difference was found statistically significant (p-value = 0.001).

Non-significant association was observed when confounding variables were compared with anxiety, depression, and MS symptoms (p-value > 0.05). When presence of anxiety (through GAD-2 scale)[7] amongst study subjects and their level of internet addiction was compared, a significant association was identified (p=0.007). Amongst those who had severe level of internet addiction, more respondents (17%) were found to have anxiety as compared to those who did not have it (6.8%) (Table-2)

Similarly, a significant association was seen (p= 0.001) while comparing presence of depression (through PHQ-2)[7] and level of internet addiction of participants. Those who had severe addiction were observed to have more number (17.7%) in depression category as compared to no depression category (5.9%). Likewise, presence of Musculoskeletal symptoms of our respondents were compared with level of internet addiction, and a significant association was established (p<0.001). Greater number of subjects was noticed to have MS symptoms (13.7%) amongst those who had severe level of internet addiction as compared to those who did not have such symptoms (9.5%) (Table-2)

Discussion

Our research quest in this descriptive, cross-sectional study aimed to find the association of depression, anxiety, and musculoskeletal symptoms with internet addiction amongst undergraduate students at King Edward Medical University, Lahore.

Habitual internet use is associated with several addictive characteristics that are analogous to symptoms of substance-use disorder including obsession, tolerance, inability to control craving, impairment of daily life activities, disregard to harmful consequences, and withdrawal.[7] In the present study, majority of the students were found to have moderate level of internet addiction (71.8%) which is contrary to the findings of Croatian study in which majority respondents had low level of internet addiction (39%).[4] This might be because we recorded data of our study during covid-19 induced lockdown in which students used internet too much for having greater availability of free time. However, another study conducted on 4211 Chinese college students showed same results i.e 17.4% of the participants were

Table 2: *: Association of anxiety, depression & MS symptoms with various levels of internet addiction (N=400)*

	Anxiety Disorder (GAD-2 score ⩾3)		Total	χ^2, df	p-value
Level of internet Addiction	**No Anxiety**	**Anxiety**			
Low level / average online user	36 (17.4%)	30 (15.4%)	66		
Moderate level	156 (75.7%)	131(67.5%)	287	10.05, 2	0.007
Severe level	14 (6.79%)	33 (17%)	47		
Total	206	194	400		
	Depression Disorder (PHQ-2 score ⩾3)		**Total**	**χ^2, df**	**p-value**
Level of internet Addiction	**No Depression**	**Depression**			
low level / average online user	36(17.7%)	30(15.2%)	66		
moderate level	155(76.3%)	132(67%)	287	13.55, 2	0.001
severe level	12(5.9%)	35(17.7%)	47		
Total	203	197	400		
	Musculoskeletal symptoms while using IT device		**Total**	**χ^2, df**	**p-value**
Level of internet Addiction	**No**	**Yes**			
low level / average online user	47(11.7%)	19(9%)	66		
moderate level	124(65.6%)	163(77.2%)	287	18.6, 2	<0.001
severe level	18(9.5%)	29(13.7%)	47		
Total	189	211	400		

considered as having moderate to severe level of Internet addiction.[9] Earlier studies did not investigate how much time the respondents spent on certain activities on the internet and did not distinguish the activities on the internet for educational purposes and leisure activities.[10,11] This shortcoming was controlled in our research by mentioning the duration for internet usage for different educational and leisure activities. In our participants, IT devices were most used for social networking system (n=167, 41.8 %). These findings are in line with a survey of 367 Turkish university students, individuals who primarily used their smart phones to access social networking sites had a significantly higher risk for smart phone addiction.[12] Similar connection was explored in 410 Hong Kong university undergraduates in which people who had cyber relationships and habit of online gambling had higher Internet addiction scores.[13]

Students recruited in our study who used IT device for the sake of e-learning and majority of them consumed 1-2 hours daily (n=107,26.8%). It was noted that highest percentage of respondents who used internet for >5 hours without any break were having severe level of internet addiction with significant p-value=0.000 which clearly showed that it is not related with e-learning. We assumed that internet addiction is responsible for the development of anxiety, depression and musculoskeletal symptoms and our data supported this hypothesis as shown by significant results.

Our findings resonate well with prior results from multiple studies which looked at the relationship between psychological traits (depression, anxiety, social phobia, loneliness) and smart phone/internet addiction. In a Lebanese study, depression (p=0.004) and anxiety scores (p=0.028) emerged as independent positive predictors of smart phone addiction, with depression score being a more powerful predictor compared to anxiety score.[7] In a sample of 440 Indian high school/college students, high prevalence of depression (85.7%) and anxiety (83.3%) in the participants addicted to the Internet was observed and was statistically significant.[14]

The relationship between greater internet usage and increased risk of musculoskeletal symptoms is widely accepted.[8,9] This exploration is consistent with our conclusions in which greater number of subjects had MS symptoms (77.2% and 13.7%) amongst those who had moderate/severe level of internet addiction with a p<0.001. We also studied the impact of proper posture on musculoskeletal symptom sand majority of the respondents who never & rarely (n= 169/287, 59%) maintained their proper posture while using IT device, had MS symptoms and this difference was statistically significant (p=0.001). Amro and his colleagues in their study also noted that only 12.9% of smart phone users and 15.7% of computer users considered proper posture recommendations while using social media on laptops and smart phones and this consideration was negatively associated with the severity of Musculoskeletal disorders in terms of severity of headache, neck, and back pain[3] which agrees with our study.

In the present study, participants were having high frequency of MSS in neck (n=166, 41.5%) followed by back (n = 131, 32.8%), shoulders (n=97, 24.3%) and hands/wrists (n=83, 20.8%). These findings are consistent with the findings of another study conducted on 150 computer users of aged 18 to 50 years in which 67 (44.7%) participants suffered from musculoskeletal problems, affecting at least one of the four anatomical sites (low back, neck, shoulder, wrist/hand). In another research conducted on 4211 Chinese youngsters, neck, shoulder, elbow, wrist/hand, low back, and waist pain was reported by participants and internet addiction was significantly related to an increased risk of musculoskeletal pain.[8]

Only 55 students (13.8%) had history of Covid-19 illness so we can say it is not proved to be a confounding variable in our study as far as anxiety, depression, and MS symptoms are concerned.

The COVID-19 induced lockdown has accelerated the implementation of e-learning and most medical schools used it regardless of their readiness. But in our study, only 52 students (13%) used IT device mostly for the sake of e-learning and majority of the students consumed only 1-2 hours. The most used e-learning sources amongst our study participants were Google Classroom and Youtube i.e 70%. When asked about their opinion regarding e-learning vs traditional learning, 60% of our students disagreed that e-learning is better than traditional learning. So, majority of our students agreed with Kaur et al[16] who concluded that regarding convenience, interaction level, individual learning needs, and balancing of practical and theoretical knowledge, the students found e-learning to be less effective than traditional learning. However, AlQhtani and his colleagues concluded that e-learning was more or equally effective in following parameters such as assignment submission and meeting individual needs, but less effective in including building skills and knowledge, and interaction level. So, they stressed on blended teaching.[17]

Conclusion

Various levels of internet addiction among study participants showed significant association with anxiety, depression, and musculoskeletal symptoms during covid-19 induced lock down. Moreover, greater number of students with severe level of internet addiction developed anxiety, depression, and musculoskeletal symptoms during this period.

Conflict of Interest: None

References

1. Khalili-Mahani N, Smyrnova A, Kakinami L. To each stress its own screen: A cross-sectional survey of the patterns of stress and various screen uses in relation to self-admitted screen addiction. J Med Internet Res. 2019;21(4):1–20.
2. Abouammoh N, Irfan F, Alfaris E. Stress coping strategies among medical students and trainees in Saudi Arabia: A qualitative study. BMC Med Educ. 2020 Apr 22;20(1).
3. Amro A, Albakry S, Jaradat M, Khaleel M, Kharroubi T. Musculoskeletal Disorders and Association with Social Media Use Among University Students at the Quarantine Time Of COVID-19 Outbreak. Issue 1 J Phys Med Rehabil Stud. 2020;1(1):1–6.
4. Černja I, Vejmelka L, Rajter M. Internet addiction test: Croatian preliminary study. BMC Psychiatry. 2019 Dec 5;19(1).
5. Dockrell S, Bennett K, Culleton-Quinn E. Computer use and musculoskeletal symptoms among undergraduate university students. Comput Educ. 2015 Jul 1; 85: 102–9.
6. Obembe AO, Johnson OE, Tanimowo TO, Onigbinde AT, Emechete AA. Musculoskeletal pain among undergraduate laptop users in a Nigerian University. J Back Musculoskelet Rehabil. 2013;26(4):389–95.
7. Matar Boumosleh J, Jaalouk D. Depression, anxiety, and smartphone addiction in university students- A cross sectional study. PLoS One. 2017;12(8):1–14.
8. Yang SY, Chen M De, Huang YC, Lin CY, Chang JH. Association Between Smartphone Use and Musculoskeletal Discomfort in Adolescent Students. J Community Health. 2017 Jun 1;42(3):423–30.
9. Yang G, Cao J, Li Y, Cheng P, Liu B, Hao Z, et al. Association Between Internet Addiction and the Risk of Musculoskeletal Pain in Chinese College Freshmen – A Cross-Sectional Study. Front Psychol. 2019 Sep 3; 10:1–7.
10. Davis RA, Flett GL, Besser A. Validation of a new scale for measuring problematic internet use: Implications for pre-employment screening. Cyberpsychology Behav. 2002 Aug;5(4):331–45.
11. Leung L. Net-generation attributes and seductive properties of the internet as predictors of online activities and internet addiction. Cyberpsychology Behav. 2004 Jun;7(3):333–48.
12. Enez Darcin A, Kose S, Noyan CO, Nurmedov S, Yılmaz O, Dilbaz N. Smartphone addiction and its relationship with social anxiety and loneliness. Behav Inf Technol. 2016 Jul 2;35(7):520–5.
13. Chang MK, Man Law SP. Factor structure for Young's Internet Addiction Test: A confirmatory study. Comput Human Behav. 2008 Sep 17;24(6):2597–619.
14. Saikia AM, Das J, Barman P, Bharali MD. Internet Addiction and its Relationships with Depression, Anxiety, and Stress in Urban Adolescents of Kamrup District, Assam. J Family Community Med. 2019; 26(2): 108–12.
15. Hellström C, Nilsson KW, Leppert J, Åslund C. Effects of adolescent online gaming time and motives on depressive, musculoskeletal, and psychosomatic symptoms. Ups J Med Sci. 2015 Oct 2;120(4):263–75.
16. Kaur N, Dwivedi D, Arora J, Gandhi A. Study of the effectiveness of e-learning to conventional teaching in medical undergraduates amid COVID-19 pandemic. Natl J Physiol Pharm Pharmacol. 2020;10(7):1.
17. Dodiya D, Vadasmiya D, Diwan J. A comparative study of flip classroom teaching method versus traditional classroom teaching method in undergraduate medical students in physiology. Natl J Physiol Pharm Pharmacol. 2019; 9:551–5.

Authors Contribution

NAW, MR: Conceptualization of Project
MR: Data Collection
NAW, MR, AI, IA, RA, KQ : Literature Search
NAW: Statistical Analysis
NAW, MR, AI, IA, RA, KQ: Drafting, Revision
NAW, MR, AI, IA, RA: Writing of Manuscript

Evaluation of Cutting Seton as A Surgical Treatment for High Anorectal Fistula-a Retrospective Observational Study

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Abstract

Objective: To determine the frequency of postoperative fecal incontinence and recurrence in patients with high anorectal fistulae after surgical treatment using Polypropylene as a cutting Seton.

Method: The retrospective observational single center study was conducted at Department of Surgery, Service Hospital, Lahore from September, 2018 to September, 2020. After applying inclusion criteria, data of 170 patients were reviewed for postoperative fecal incontinence and recurrence.

Results: The mean age of patients was 41.59 ± 7.61 years with minimum and maximum age as 15 and 50 years. There were 99 (58.2%) male and 71(41.8%) female cases. The mean duration of fistula was 8.03 ± 1.39 weeks with minimum and maximum duration as 6 and 10 weeks. Patients were followed up for two years, 5 (2.9%) patients had recurrence and 2 (1.4%) cases had fecal incontinence.

Conclusion: The frequency of postoperative fecal incontinence and recurrence in patients with high anorectal fistulae after surgical treatment using Polypropylene as a cutting seton was minimal, hence, cutting setone seems to be an effective and relatively safe treatment for high anal fistula with low rate of incontinence.

Keywords: Fecal incontinence, recurrence, high anorectal fistulae, Polypropylene, cutting seton

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Introduction

Anorectal fistula is an abnormal passage which is lined by granulation tissue, connecting two epithelium lined surfaces, anorectal lumen and skin.[1] Majority of fistulas arise as chronic sequelae of anorectal suppuration in which anal crypt glands present at the level of dentate line in inter sphincteric plane are infected.[2] After surgical or spontaneous drainage in the perianal skin, a granulation tissue–lined tract is occasionally left behind, causing recurrent symptoms. Other fistulas develop secondary to trauma (e.g. rectal foreign bodies), Crohn's disease, carcinoma, anal fissures, radiation therapy.[3]

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In high fistulae primary opening originates above the dentate line and puborectalis with fistulous tract involving more than 30% of internal sphincter muscle fibers.[4] Management of high variety of anorectal fistulae requires balance between the eradication of sepsis and preservation of continence. Cutting Seton consists of a non-absorbable suture or a rubber band that is placed through the internal and external opening of the fistula and intermittently tightened.[5]

Tightening the seton results in gradual division and fibrosis of the sphincter, thus eliminating the fistula while maintaining continuity of the sphincter. Using Seton is associated with the least rate of complications such as incontinence and recurrence.[6] Despite the presence of already conducted work on this topic, there is conflict in results between international and local literature.[7,8] In a study conducted in the D. I. Khan, it was observed that recurrent fistula was noted in one patient (3.3%) at 5 months while none (0%) developed incontinence.[8] Another study found that postoperative fecal incontinence in 0% cases as well as no fistula recurrence

occurred with cutting seton with healing rate 100%.[7] While in an Egyptian study, it was reported that recurrence rate was 9.8% while no fecal incontinence observed.[2]

Therefore, we retrospectively analyzed the data of patients that were managed with cutting seton at the Department of Surgery, SIMS Lahore. Patients with high anorectal fistulae were operated from September, 2018 to September, 2020. On the basis of findings of this study, it is presumed that current practice guidelines can be updated for successful treatment of high anal fistula.

Cutting Setons

Cutting Setons are used by securing the Seton tightly within the fistula tract with purposeful pressure on the tract itself. The Seton can then be serially tightened in the office over time. This is a general high school science phenomenon in which a paper clip or wire is applied on an ice chunk and this ice piece maintain its shape as the wire progresses.[9] Flatus incontinence is most common with 12-26% of incontinence rate of stool accompanied by liquid stool.[10,11] Previous studies indicated the average rate flatus incontinence should be 9.7% and solid stool is 5%.

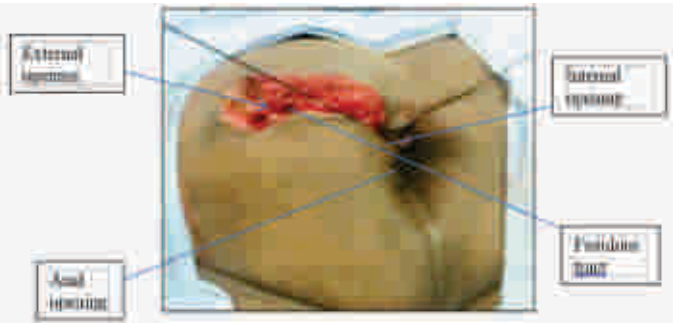

Fig 1: *Application of Cutting Seton 58*

Material and Methods

The study was a mono-center retrospective observational study conducted in Department of Surgery, SIMS Lahore from September, 2018 to September, 2020. All the surgical procedures were performed in a single surgical unit by the same surgeon (associate professor). After reviewing the database of the Hospital, only 170 patients were fitted in the selection criteria. Inclusion criteria was age between 15-50 years both genders and patients with high anorectal fistulae, patients excluded were with recurrent fistulae, Immuno-compromised, previous history of irradiation or on steroid during last 2 weeks. The anthropometric data, history of smoking, diabetes mellitus and duration of fistula were noted. Patients in the cohort were operated using Seton (Prolene No. 1), under general or spinal anesthesia. Metallic Probe was gently passed through the fistulous tract. Elliptical incision around the external opening was made, tract outside the sphincters were dissected and excised. The Seton (Prolene No.1) was then passed through the remaining tract and tied over itself on the sphincter muscles. Postoperatively patients were advised to take Sitz-bath, with oral ciprofloxacin and metronidazole for 7 days. Follow up on a weekly basis for the tightening of Seton was carried out, till the Seton drops by itself. After 1 month of Seton drop patients were contacted to assess the fecal incontinence and recurrence. Data were analyzed using SPSS for windows (Version 22.0 IBM Corp, Armonk, USA). The normal distributions of data were assessed using Kolmogorov Smirnov test Means and standard deviation were calculated for quantitative variables like age, BMI and duration of fistula. For qualitative variables (gender, diabetes, smoking, postoperative recurrence and fecal incontinence), data were expressed as frequency and percentage. Data were further stratified for age, gender, BMI, diabetes, smoking, and duration of Seton drop to control effect modifiers. Chi-square test was applied to compare outcome in stratified groups. Significance level was predetermined at $p \leq 0.05$.

Results

Mean age of patients was 41.59 ± 7.61 years ranging from 15 to 50 years. The mean BMI was 27.95 ± 3.21 ranging from 22 to 34. The mean duration of fistula was 8.03 ± 1.39 weeks (range: 6 and 10 weeks). Only twenty-one (12.4%) patients were 15-35 years-old and 149 (87.6%) were 36-50 years-old. Data showed that our cohort was predominantly comprised of males than the females. Only 50 (29.4%) patients had diabetes mellitus. Fifty-two (30.6%) patients were smokers. A total of 89 (52.4%) patients had duration of seton drop as <10 days and 81(47.6%) had seton drop as 10-30 days (Table 1). Only 5 (2.9%) patients had postoperative recurrence and 2 (1.4%) patients had fecal incontinence (Table 1). When data was stratified for age, gender, smoking, BMI and duration of seton drop, the frequency of postoperative recurrence and fecal incontinence was statistically similar in all strata (Tables 2, 3).

Table 1: *Frequency distribution of patients (n = 170)*

Characteristics	Number of patients
Age (years)	
15-35 years	21
36-50 years	149
Gender	
Male	99
Female	71
History of Diabetes Mellitus	
Yes	50
No	120
History of Smoking	
Yes	52
No	118
Duration of Seton Drops	
<10 days	89
10-30 days	81
Post-operative recurrence	
Yes	5
No	165
Fecal Incontinence	
Present	2
Absent	158

Table 2: *Comparisons of Postoperative Recurrence with Respect to Multiple Factors*

Factor		Postoperative Recurrence		
		Yes (%)	No (%)	P-Value
Age (Years)	15-35	1(4.8%)	20(95.2%)	0.598
	36-50	4(2.7%)	145(97.3%)	
	Total	5(2.9%)	165(97.1%)	
Gender	Male	2(2%)	97(98%)	0.401
	Female	3(4.2%)	68(95.8)	
	Total	5(2.9%)	165(97.1)	
Body Mass Index (Kg/m^2)	Obese	1(2.1%)	47(97.9%)	0.678
	Non-Obese	4(3.3%)	118(96.7)	
	Total	5(2.9%)	165(97.1%)	
History of Diabetes Mellitus	Yes	1(2%)	49(98%)	0.639
	No	4(3.3%)	116(96.7%)	
	Total	5(2.9%)	165(97.1)	
History of Smoking	Yes	2(3.8%)	50(96.2%)	0.643
	No	3(2.5%)	115(97.5%)	
	Total	5(2.9%)	165(97.1%)	
Duration of Seton drop (days)	<10 days	3(3.4%)	86(96.6%)	0.728
	10-30 days	2(2.5%)	79(97.5%)	
	Total	5(2.9%)	165(97.1%)	

Table 3: *Comparisons of Fecal Incontinence with respect to multiple factors*

Factor		Fecal incontinence		
		Yes	No	P-Value
Age (years)	15-35	1(4.8%)	20(95.2%)	0.816
	36-50	9(6%)	140(94%)	
	Total	10(5.9%)	160(94.1%)	
Gender	Male	6(6.1%)	93(93.9%)	0.907
	Female	4(5.6%)	67(94.4)	
	Total	10(5.9%)	160(94.1%)	
Body Mass Index (Kg/m^2)	Obese	2(4.2%)	46(95.8%)	0.551
	Non-Obese	8(6.6%)	114(93.4%)	
	Total	10(5.9%)	160(94.1%)	
History of Diabetes Mellitus	Yes	2(4%)	48(96%)	0.501
	No	8(6.7%)	112(93.3%)	
	Total	10(5.9%)	160(94.1%)	
History of Smoking	Yes	4(7.7%)	48(92.3%)	0.506
	No	6(5.1%)	112(94.9%)	
	Total	10(5.9%)	160(94.1%)	
Duration of Seton drop (days)	<10 days	3(3.4%)	86(96.6%)	0.145
	10-30 days	7(8.6%)	74(91.4%)	
	Total	10(5.9%)	160(94.1%)	

Discussion

In almost 80% of cases, anal fistula arises as secondary condition to abscess coming from affected anal glands.[10] High and low classification depends upon the height of the tract as it navigates from the sphincter muscle rather point of internal opening which is almost at the dentate line.[12] There are many options for the treatment of anal fistula which include fistulotomy, seton application, fistula plug, ligation of the inter sphincteric fistula tract, anorectal advancement flap, dermal island flap, and fibrin injection.[12] Seton is a string type substance which is tied after passing through the fistula tract and initiate the inflammatory and fibrotic process to save and avoid retraction of sphincter upon its division. So, it helps to retain the continuity of sphincter during cutting procedure.[13] There are different types of Setons including braided polyester, nylon, rubber bands, silk, polypropylene. Among these, the proline seton is less expensive, provide convenient tightening, and can be applied easily in a clinic without use of analgesia.[14] Different types of seton have recurrence rate range from 0-16% with an incontinence rate of 0-62%.[10,15]

The cutting seton is also a string like substance which is applied in fistula tract and tightened gradually. It results into slow transection of the external sphincter which leads to pressure necrosis with an insignificant splitting

of the cut ends. Thus, it can restore the continuity during the cutting procedure.[14]

A prospective study from January 2005 to December 2014 was carried out on 372 patients with high anal fistula using 0-silk as cutting seton at Al- Asar General Hospital, Madina. Seton was tightened on weekly basis in outpatient clinics. Results revealed 298 (80.1%) males and 74(19.9%) females. Symptoms varied from 3-12 months. Full healing in 363 (97.6%) patients,58 (15.6%) had incontinence to flatus, none had to feces and 9 (2.4%) had recurrence. Hence, use of the cutting seton for high anal fistula is very effective as it instantaneously evacuates the abscess, cuts the tract of fistula, and make fibrosis on tract.[16] In the present study, we have found a higher percentage of male and other signs were comparable. Another study examined the efficacy of seton in High anal fistula, average age of the patients was 38.2±6.8 years in 57 cases.51 cases showed complete healing of fistula and 2 patients had incontinence while the recurrence was observed in 4 patients. Therefore, it can be assumed that the use of seton is comparatively safer, cheaper, and efficient solution for controlling the high anal Fistula with low rate of incontinence. Hence it can be suggested as standard treatment for the control of high anorectal fistula.[12] In another study of 2017, 68 patients (59 males and 9 females) were treated with cutting seton and followed for 12 months. Results revealed complete recovery in 55 (80.9%) unsuccessful in 13(19.1%), 9 patients (13.2%) reported slight incontinence, 6 (8.8%) to gas, 3 (4.4%) to liquid stools but none reported solid stool incontinence. Recurrence was observed in 2 patients (2.9%). Hence, it was concluded that the use of cutting seton have fairly good results regarding the treatment of fistula and have better continence in most of the cases, however, the failure risks were quite high so the use of cutting seton is not recommended in all cases of anal fistulas.[17] In another descriptive study of 2016 at Al-Hada Armed Forces hospital, Taif, 51 patients were treated with cutting seton during December 2012 to December 2013. Results showed incontinence to flatus was 15.7%, incontinence to liquid stool was 5.9%, recurrence rate 9.8%. However, incontinence for solid was zero. Hence, it is suggested that cutting setons are right treatment for complete recovery of anorectal fistula. However, other options of surgery are advised for the females and those patients which have gone through any kind of previous surgery.[18]

In another research eighteen patients comprises of 16 males and 2 females with fistula above dentate line and involvement of more than 30% internal sphincter were subjected to treatment with cutting seton for a duration of 3 years. Follow-up for fistula recurrence, incontinence, and degree of satisfaction was done. Results demonstrated postoperative incontinence in 4 of 18 patients (22.2%) gas incontinence in 3 patients (16.6%) and liquid stool incontinence in 1 patient (5.6%) and none had solid stool incontinence. There was no fistula recurrence with healing rate 100%. SO, the study concluded that cutting Seton is an effective and relatively safe management of high anal fistula with low rate of incontinence.[7] Another study was conducted to find out the recurrence rate and fecal incontinence in anorectal fistula, treated with cutting seton using polypropylene. Study involved 30 patients with high anorectal fistula treated from April 2011 to March 2014 at Mufti Mehmood Memorial Teaching Hospital, D.I. Khan.

Patients were followed for six months to monitor the recurrence, full recovery, and anal incontinence. Out of 30 patients, average age was 40 years with range of 20-66 years, full recovery took three months in all patients (100%). At 5 months, only 1(3.3%) patient reported recurrent fistula and none reported incontinence. Therefore, surgical treatment of anorectal fistula with cutting seton was linked with lower rate of anomalies. Hence, it can be suggested as standard treatment for anorectal fistula.[8] In another recent study of Sudan published in 2022, patients (n=72) were treated with cutting seton for high trans-sphincteric fistula. Results revealed that 70% patients were male. Forty-eight (66.7%) patients required two sessions of seton tightening with a duration of seton treatment of 30 days and 24 (33.3%) patients required three sessions with a duration of seton treatment of 45 days. Flatus incontinence and fistula recurrence were noted in 1.4% and 2.8% patients respectively. Twenty-six (36%) patients achieved complete healing within 30 days, while 36 (54.3%) patients healed within 60 days.[19]

Conclusion

It is concluded that the frequency of postoperative fecal incontinence and recurrence in patients with high variety of anorectal fistulae after surgical management using Polypropylene as a cutting seton was minimal. Therefore, it appears that cutting seton is an effective and relatively safe treatment of high anal fistula with low rate of incontinence.

Conflicts of Interest None

References

1. Farag AFA, Elbarmelgi MY, Mostafa M, Mashhour AN. One stage fistulectomy for high anal fistula with reconstruction of anal sphincter without fecal diversion. Asian J Surg 2019; 42(8):792-796.
2. Raslan SM, Aladwani M, Alsanea N. Evaluation of the cutting seton as a method of treatment for perianal fistula. Annals of Saudi medicine. 2016; 36(3):210-5.
3. Papaconstantinou I, Kontis E, Koutoulidis V, Mantzaris G, Vassiliou I. Surgical management of fistula-in-ano among patients with Crohn's disease: analysis of outcomes after fistulotomy or seton placement– single-center experience. Scand J Surg. 2017; 106(3):211-5.
4. Morsi AEF. Study of the outcome of staged cutting seton in treatment of high perianal fistula. Egyp J Hospital Med. 2019; 74(7):1631-5.
5. Gold SL, Cohen-Mekelburg S, Schneider Y, Steinlauf A. Perianal fistulas in patients With Crohn's disease, Part 2:surgical, endoscopic, and future therapies. Gastroenterol Hepatol. 2018; 14(9):521.
6. Corman ML, Bergamaschi RC, Nicholls RJ, Fazio VW. Corman's Colon and Rectal Surgery. 6th ed. New York Lippincott Williams and Wilkins; 2013
7. Mogahed M, Elwakeel B, Boraii S. Cutting Seton as surgical management of high anal fistula. Al-Azhar Assiut Medical Journal. 2015; 13(2).10-14.
8. Munir A, Falah SQ. Management of high fistula in ano with cutting seton. Gomal J Med Sci. 2014; 12(4). 210-212.
9. Bubbers EJ, Cologne KG. Management of complex anal fistulas. Clin Colon Rectal Surg. 2016; 29(1):43-45.
10. Ritchie R, Sackier J, Hodde J. Incontinence rates after cutting seton treatment for anal fistula. Colorectal Dis. 2009; 11(6):564-71.
11. Chuang-Wei C, Chang-Chieh W, Cheng-Wen H, Tsai-Yu L, Chun-Che F, Shu-Wen J. Cutting seton for complex anal fistulas. Surgeon. 2008; 6(3):185-8.
12. Alam MNA, Abbasi S. Use of Seton in management of high variety of anal fistula. Anwer Khan Mod Med Coll J. 2017; 8(2):100-4.
13. Thomson J, Ross AM. Can the external anal sphincter be preserved in the treatment of trans-sphincteric fistula-in-ano? Int J Colorectal Dis. 1989; 4(4):247-50.
14. Eitan A, Koliada M, Bickel A. The use of the loose seton technique as a definitive treatment for recurrent and persistent high trans- sphincteric anal fistulas: a long-term outcome. J Gastrointest Surg. 2009; 13(6):1116-9.
15. Vial M, Parés D, Pera M, Grande L. Faecal incontinence after seton treatment for anal fistulae with and without surgical division of internal anal sphincter: a systematic review. Colorectal Dis. 2010; 12(3):172-8.
16. Shirah BH, Shirah HA. The impact of the outcome of treating a high anal fistula by using a cutting seton and staged fistulotomy on saudi arabian patients. Ann Coloproctol. 2018; 34(5):234-240.
17. Al-Marzooq TJ, Hassan QA, Alnaser MK, Al-Edani MS. Treatment of Fistula-In-Ano with Tight (Cutting) Seton: Analysis of Outcomes and Efficacy Assessment. J Clin Diagn Res. 2017; 11(11):5-8.
18. Raslan SM, Aladwani M, Alsanea N. Evaluation of the cutting seton as a method of treatment for perianal fistula. Ann Saudi Med. 2016; 36(3):210-5.
19. Ali, ALKE, Wong, MP-K, Sagap, I. The value of cutting seton for high transsphincteric anal fistula in the era of Its misery. Mal J Med Sci. 2022; 29 (1) 55-61.

Authors Contribution

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

Comparison of Monopolar Electrocautery Versus Harmonic Scalpel in Dissection of The Gall Bladder from Gallbladder Bed in Laparoscopic Cholecystectomy

Maliha Javaid Butt,[1] Muhammad Adil Iftikhar,[2] Usman Ali Rahman,[3] Humaira Yousaf,[4] Iftikhar Ahmed,[5] Ali Asad[6]

Abstract

Objective: The objective of this study was to compare the incidence of gall bladder perforation during its dissection with monopolar electrocautery Vs harmonic scalpel from liver bed in laparoscopic cholecystectomy.

Method: It was a comparative study held at Surgical Department, surgical department, Services Hospital, Lahore to check the incidence of gallbladder perforation and difference in duration of procedure during gall bladder dissection with harmonic versus monopolar electrocautery. Total 144 patients under laparoscopic cholecystectomy for symptomatic gall stone disease in surgical department of Services Hospital, Lahore were included in this study and divided in two groups. In group A gall bladder dissection was done with monopolar electrocautery while in group B harmonic scalpel was used.

Results: Incidence of perforation in laparoscopic cholecystectomy done with monopolar electrocautery and harmonic scalpel was 16.6 % vs 15.3% and operative time was 46.38±14.04 minutes vs 19.36± 4.96 minutes.

Conclusion: Incidence of perforation of gall bladder is almost equal during its dissection from liver bed when done either with monopolar electrocautery or harmonic scalpel with the duration of procedure making the difference between the two groups.

Keywords: laparoscopic cholecystectomy, harmonic scalpel, monopolar electrocautery.

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Introduction

Removal of gall bladder is known as cholecystectomy.1 It is the most common surgical procedure worldwide. Carl August Langenbuch in 1882 performed first Laparoscopic cholecystectomy. In Pakistan first Laparoscopic cholecystectomy was performed in 1991. Inflammation of gall bladder is known as cholecystitis which most commonly occurs in the presence of gall stones.[2] Patients of acute cholecystitis usually presents with repeated attacks of pain at right hypochondrium and epigastrium. This pain is associated with nausea, vomiting, dyspepsia, indigestion, flatulence, and abdominal distension. Cholecystectomy is the management of choice for cholelithiasis. It is usually done by open and laparoscopic technique. Cholecystectomy is associated with post-operative complications of pain, nausea, vomiting and wound infection.

Laparoscopic cholecystectomy is considered better as compared to open due to significant reduction in post-operative pain, shorter hospital stay and early recovery.[3] It results in patient's earlier return to normal life and work activities. Now a days in experienced hands operation is done as an outpatient procedure in appropriately selected patients.

Different instruments are used for dissection of gall bladder from gall bladder fossa. These include monopolar electrocautery and ultrasonic dissector. Gall bladder

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perforation is associated with spillage of bile and stones in abdominal cavity during dissection. It disrupts flow of surgery and also increase operative time. It may also results in increased postoperative intra peritoneal infections which increase not only morbidity but also mortality rate of patients. Reported incidence of gall bladder perforation during surgery is 20–40%.[4] Currently gall bladder is removed from gall bladder fossa using monopolar electrocautery. Complication includes local and distant tissue damage by heat.

Ultrasonic dissection is now done for gall bladder removal in some setups. This technique is safer due to less thermal injury, creation of smaller zone of tissue damage and more accurate dissection. In some international studies incidence of gallbladder perforation is reported low with ultrasonic dissection compared to monopolar electrocautery during laparoscopic cholecystectomy.[5]

The present study was designed and conducted to determine and compare electrocautery with ultrasonic dissector for gall bladder dissection in laparoscopic cholecystectomy and to determine the incidence of gallbladder perforation during dissection.

Material and Methods

Comparative study was carried out in 6 months from July to December 2020. Inclusion criteria includes patients with age between 16-80 years. Exclusion criteria includes patients with co morbidities, acute cholecystitis and liver cirrhosis. Patient from Services Hospital were selected that were having no comorbidity like hypertension, diabetes, HIV or hepatitis B, C etc and data was documented on prescribed questionnaire after getting permission from Institute Review Board (IRB). Informed patient consent was taken prior to getting information. They were also informed about associated risks with their operation and they were purposively selected for both procedures based on patient's availability and surgeon's willingness for fulfilling the inclusion criteria. All the procedures were performed by consultant surgeons. Sample size was calculated by considering reference study[6] using epi-info software and based on population undergoing surgery in our Hospital with 95% Confidence level and 5% error rate. It was 72 in number for each case i.e. Group A (monopolar electrocautery) and Group B (Harmonic Scalpel). Patients were then randomly allocated into two groups A and B by using random numbers table method. In group A gall bladder dissection was done with the help of monopolar cautery and in group B gall bladder dissection was carried out with the help of harmonic scalpel. The rate of gall bladder perforation was noted in both groups. All cases included in the study were operated under general anesthesia. Demographic information of patient (name, age, sex) was obtained along with informed patient consent prior to anesthesia. Data was analyzed using SPSS version 23 through its statistical program. The variable under study were gall bladder perforation and operative time. The gall bladder perforation was considered positive in case of bile leakage from gall bladder during dissection. Operative time was noted from callot's triangle dissection to gall bladder removal from liver bed. This variable was analyzed using simple descriptive statistics, using mean and standard deviation. The significance of differences observed by the two methods being mainly qualitative (gall bladder wall perforation) were subjected to Chi Square test. A p value of 0.05 or less was taken as criteria of significant results. Data of other variables was stratified for age, gender, number of stones (single and multiple) and duration of symptoms to address effect modifiers. Chi square test was applied post stratification with p-value ≤ 0.05 taken as significant.

Results

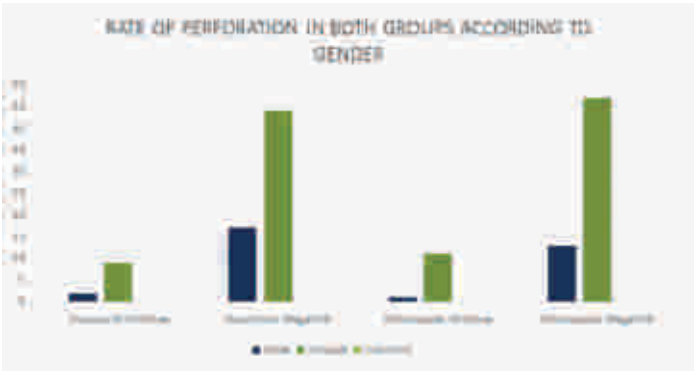
It was found that patients in Group A were 58/72 (80.6%) female and 14/72 (19.4%) male whereas in Group B 53/72 (73.6%) were female and 19/72 (26.4%) were male. The age of the study subjects in group A was comprised of age range of 24-65 years with mean of 38.22±8.30 years and in group B age range was 17-75 years with mean 35.68±7.41years. The pre-operative ultrasound showed multiple stones in gall bladder in all patients of both groups. Stone duration from patients were asked and found that patients had mean value of 14.06±6.08 months in group A while patients of group B had stones with mean value of 15.56±6.84 months

Table 1: *Presentation of statistical analysis of gall bladder perforation in both study groups*

Study Variables		Group A gall bladder dissection was done with the help of monopolar cautery n=72		Group B gall bladder dissection was carried out with the help of harmonic scalpel n=72		P- Value
		Number	Percentage	Number	Percentage	
Perfotion	Positive	12	16.6	11	15.3	0.84
	Negative	60	83.4	61	84.7	

Chi square showed P-Value of 0.587. Operative time for surgical procedures was calculated and it was found that for group A mean value was 46.38±14.04 minutes and for group B mean value was comprised of 19.36± 4.96 minutes. Chi square was applied and p-value was calculated that showed 0.630 for comparing both the cases. Conversion rate to open cholecystectomy was nil and similarly no intraoperative or immediate postoperative complication was reported. Perforation of gall bladder was reported in 12/72 (16.6%) cases of group A whereas 11/72 (15.3%) in group B as shown in Table 1. Perforation within both groups have been shown in (Fig-1).

Fig-1. *Graphical Presentation of Association of Gender with Perforation in both Study Groups*



Discussion

Cholelithiasis is the commonest medical problem that results in surgical intervention. The confounding variables include obesity, hemolytic diseases and cirrhosis but such cases were excluded from the sample.

Although this comparative study did not show significant p-values for determining any relationship between presence of perforation due to usage of scalpel in both study groups but found harmonic scalpel as more effective and safer for removal of gallbladder from liver bed than monopolar cautery as using monopolar cautery cases were presented with relatively high rate of perforation with 16.6% as compared to those performed with harmonic scalpel that resulted in 15.3% cases of peroration. This study confirms with the findings of previous studies who found harmonic scalpel as a safer surgical instrument for gallbladder dissection preventing gall bladder perforation and decreasing operating time as compared to monopolar electrocautery.[5-7] The gall bladder perforation during surgical procedures by any of the two methods may result in lengthening of surgical procedure. Electro cautery dissection is reported for high chances of gall bladder perforation either due to being too close to the gallbladder wall or using lengthy duration of energy delivery.[8]

Cavitation and smokeless coagulation results in advantage over electro cautery for gall bladder dissection by harmonic scalpel. Effective closure of the ducts of Luschka during liver bed dissection is another advantage of Harmonic scalpel as if not done effectively it may result in postoperative pain, small bilomas, and the occasional return to the operative room.[5-7]

According to Tsimoyiannis et al gallbladder dissection using harmonic scalpel in experienced hands results in less incidence of gallbladder perforation and operative time. Inexperienced residents or surgeons who didn't have familiarity with harmonic scalpel may result in prolonged surgical procedures.

According to Wetter et al. usage of harmonic scalpel resulted in less operative time because it was used as a sole instrument that did not allow to use extraction and insertion of various instruments. This resulted also in easy handling of instruments thus minimizing the instrument handling errors and avoid wastage of time. It is reported that smoke was not produced during surgery with harmonic scalpel rather microaromized water droplets were formed. The mist generated by this method was swiftly absorbed through peritoneal surface, and did not require suctioning or releasing caused due monopolar electrocautery dissection. Thus per operatively visibility of the operative field was preserved during procedure.[9-11] Limitation of this study includes small sample size due to single center study. Large multicenter study is required to determine statistical significance in less incidence of gall bladder perforation and operative time between monopolar electrocautery and harmonic scalpel in gall bladder dissection.

Conclusion

This study concluded that both monopolar electrocautery and harmonic scalpel have equal chances of gall bladder perforation during its dissection. However there is significant reduction in operative time while using harmonic scalpel by experienced hands.

Conflict of Interest *None*

Reference

1. Clout M, Blazeby J, Rogers C, Reeves B, Lazaroo M, Avery K, Blencowe NS, Vohra R, Jennings N, Hollingworth W, Thorn J. Randomised controlled trial to establish the clinical and cost-effectiveness of expectant management versus preoperative imaging with magnetic resonance cholangiopancreatography in patients with symptomatic gallbladder disease undergoing laparoscopic cholecystectomy at low or moderate risk of common bile duct stones (The Sunflower Study): a study protocol. BMJ open. 2021 Jun 1;11(6):e044281.

2. Shukla A, Seth S, Ranjan A. A comparative study between laparoscopic and open cholecystectomy in cases of cholecystitis with cholelithiasis: one year experience in tertiary care center. International Surgery Journal. 2017 Feb 25;4(3):903-7.
3. Manatakis DK, Papageorgiou D, Antonopoulou MI, Stamos N, Agalianos C, Ivros N, Davides D, Pechlivanides G, Kyriazanos I. Ten-year audit of safe bail-out alternatives to the critical view of safety in laparoscopic cholecystectomy. World journal of surgery. 2019 Nov; 43(11):2728-33.
4. Altuntas YE, Oncel M, Haksal M, Kement M, Gundogdu E, Aksakal N, Gezen FC. Gallbladder perforation during elective laparoscopic cholecystectomy: Incidence, risk factors, and outcomes. Northern clinics of Istanbul. 2018; 5(1):47.
5. Jiang HP, Liu YD, Li YS, Shen ZL, Ye YJ. Ultrasonic versus electrosurgical device for laparoscopic cholecystectomy: A systematic review with meta-analysis and trial sequential analysis. International journal of surgery. 2017 Apr 1;40:24-32.
6. Sanawan E, Qureshi AU, Qureshi SS, Cheema KM, Cheema MA. Effectiveness of ultrasound shear for clipless laparoscopic cholecystectomy versus conventional unipolar electrocautery in patients with cholelithiasis. Journal of the College of Physicians and Surgeons Pakistan. 2017 Oct 1;27(10):611-5.
7. Rajnish K, Sureshkumar S, Ali MS, Vijayakumar C, Sudharsanan S, Palanivel C. Harmonic scalpel-assisted laparoscopic cholecystectomy vs. conventional laparoscopic cholecystectomy-a non-randomized control trial. Cureus. 2018 Jan;10(1).
8. Rosenberg J, Leinskold T. Dome down laparosonic cholecystectomy. Scandinavian journal of surgery. 2004; 93(1):48-51.
9. Kandil T, El Nakeeb A, El Hefnawy E. Comparative study between clipless laparoscopic cholecystectomy by harmonic scalpel versus conventional method: a prospective randomized study. Journal of Gastrointestinal Surgery. 2010;14(2):323-8.
10. Choi C, Do IG, Song T. Ultrasonic versus monopolar energy-based surgical devices in terms of surgical smoke and lateral thermal damage (ULMOST): a randomized controlled trial. Surgical endoscopy. 2018 Nov; 32(11): 4415-21.
11. Amudhan Kannan AT, Quadir H, Hakobyan K, Gaddam M, Ojinnaka U, Ahmed Z, Dominic JL, Kantamaneni K, Went TR, Mostafa JA. The Outcomes of the Patients Undergoing Harmonic Scalpel Laparoscopic Cholecystectomy. Cureus. 2021 Jun;13(6).

Authors Contribution

MJB: Conceptualization of Project
MAI: Data Collection
UAR: Literature Search
HY: Statistical Analysis
IA: Drafting, Revision
AA: Writing of Manuscript

Original Article

Impact of Hirsutism on Quality of Life of Patients Using Dermatology Life Quality Index

Ayesha Saleem,[1] Hira Tariq,[2] Saadiya Siddiqui,[3] Shahbaz Aman[4]

Abstract

Objective: To assess the effect of hirsutism on everyday life of patients using Dermatology Life Quality Index (DLQI) score

Method: This cross-sectional survey was conducted at Dermatology Outpatient Department of Services Hospital, Lahore for six months. 132 patients of hirsutism were enrolled. Demographic details of patients were noted and extent and severity of disease were assessed by physical examination. DLQI questionnaires in Urdu were filled in by the patients. Total scores were calculated and impact on everyday life was noted as No effect (0-1), Minimal effect (2-5), Modest effect (6-10), Very huge effect (11-20) and Extremely huge effect (21-30).

Results: Mean age of patients was 25.47±2.83 years. 65 patients (49.2%) were in 16-25 years age group, while 67(50.8%) were in 26-40 years age group. According to severity of disease, 52(39.4%) had mild, while 42(31.8%) and 38(28.8%) had moderate and severe disease respectively. Mean DLQI score among hirsutism patients was 10.78±5.99. According to stratification of DLQI score with respect to different variables, high DLQI score was significantly associated with higher education and severe disease. Impact of disease on everyday life was noted as: No effect on 1 patient (0.7%), Small effect on 34 patients (25.8%), Moderate effect on 33 patients (25%), Very large effect on 55 patients (42.4%) and Extremely large impact on everyday life of 8 patients (6.1%).

Conclusion: Hirsutism can significantly impair women's everyday life as most of the patients reported modest to massive impairment of daily life functionality. So, patients tolerating this infirmity should be treated with courtesy and civility.

Keywords : Hirsutism, Quality of life, Dermatology Life Quality Index (DLQI)

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Introduction

Hirsutism refers to presence of excess terminal hair in women at sites where males have excess hair under the influence of male hormones including upper lips, beard, trunk, etc. It is not an uncommon disorder with a prevalence of around 10-20%. Polycystic ovarian syndrome (PCOS) is one of the commonest causes.[1] Other causes include Hypothyroidism, Congenital Adrenal Hyperplasia (CAH) and Hyperandrogenic Insulin Resistant Acanthosis Nigricans Syndrome (HAIR-AN). Idiopathic hirsutism accounts for 40% of cases.[2] The disease has an immense effect on psychological and social wellbeing of patients particularly when associated with PCOS probably because associated hyperandrogenic state and dysmetabolic syndrome. The longstanding course of the disease and unavailability of effective cure is frustrating for both sufferers and their families. This leads to significant psychosocial infirmity due to unsightly appearance of face and body

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and reduced confidence amongst hirsute women.[3]

Quality of life is a measurable tool which is multidimensional index of social, behavioural and cultural factors. The Dermatology Life Quality Index (DLQI) score was proposed by Finlay et al. in 1994 and is used to estimate the impact of disease on everyday life of sufferers.[4] This 10-item questionnaire was applied in many studies, its validity and reliability in cutaneous disorders is proven.[5,6] The psychosocial issues reported in hirsutism include aggression, jealousy, frustration, avoiding people, difficulty in socializing etc.[7] The inferiority complex faced by hirsute women is further aggravated by the cost of cosmetics and expensive treatments of hirsutism.[8] This survey was designed to analyse the impact of disease on daily life of hirsute women in our population and to assess the psychological impact on patient`s personal and social life. By knowing the magnitude of the problem, Dermatologists can have a significant role in reducing the anxiety and misery of patients and help them better cope with their appearance and psychosocial issues. This may eventually lead to better management of this psychosomatic disorder.

Methods

After getting approval from Ethical Review Board, patient selection was done by non-probability consecutive sampling from the Outpatient Department of Dermatology, Services Hospital, Lahore from February 2021 to August 2021. Females of ages between 16 and 40 years, who were diagnosed cases of Hirsutism on basis of presence of terminal hair on androgen dependent areas of body for more than six months. Patients who were excluded from the study were; psychiatric patients who couldn't answer the questionnaire properly, patients taking psychoactive drugs and patients having any other co-existing chronic dermatological or medical illnesses such as diabetes mellitus, hypertension, peripheral vascular disease etc which may contribute to altered quality of life.

After taking written informed consent, 132 patients of hirsutism were enrolled. Their demographic data was registered on predesigned proformas. The severity and extent of disease was noted by physical examination using Modified Ferriman–Gallwey (mFG) score. An mFG score ≥ 8 constitute hirsutism. Then, severity of hirsutism was analysed as: one-area limited hirsutism (mFG score <8), mild (8-10), moderate (11-14) and severe (>15) hirsutism.9 DLQI questionnaires Urdu version was filled by the women, after explaining the purpose of research and method of filling the questionnaire. After collecting the questionnaires from patients scoring was done for each question and total score and impact on daily life of patients was noted.

DLQI questionnaire is comprised of ten queries, about various dominions of everyday activities, relations and emotions impacted upon by disease or its treatment. Each question is scored from zero to three depending on none to severe impact. The total DLQI score varies from zero to 30. Higher score reflects more impairment of everyday functionality and well-being. Overall impact on daily activities is classified as no effect at all (0 to1), minimal effect (2 to 5), modest effect 6 to 10), very large effect (11 to 20) and extremely huge effect (21 to 30).[10]

Data was entered and analysed using SPSS Vs 27. Descriptive statistics were calculated for all variables. Quantitative variables including age, duration of disease and DLQI scores were expressed as mean and standard deviation. Qualitative variables including education, occupation, socio-economic status, severity of disease and effect (No, Mild, Moderate, very large or Extremely large effect) on quality of life of patients were expressed as frequency and percentages. Data was stratified with respect to age, education, occupation, socio-economic status, severity and duration of disease. Post-stratification, results were analysed using student t-test. A p-value of ≤0.05 was considered statistically significant.

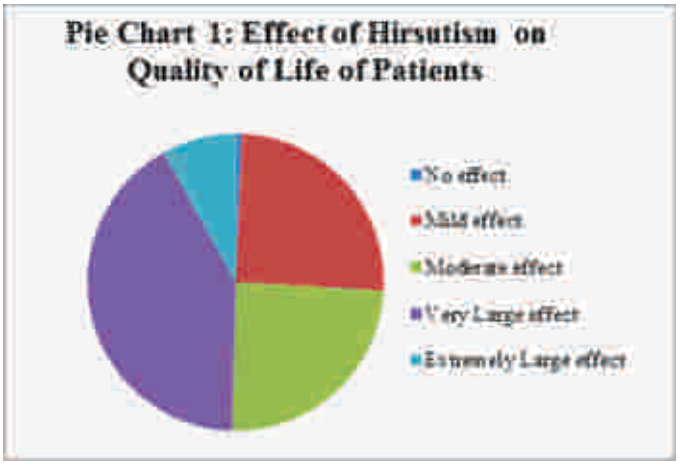
Results

A total of 132 patients were included in the study during the study period of six months. Mean age of the patients was 25.47±2.83 years. Out of total, 65(49.2%) were in 16-25 years age group, while 67 (50.8%) were in 26-40 years age group. As far as socio-economic status was concerned, 43(32.6%) had low income, while 41(31.1%) and 48(36.3%) belonged to middle and upper class respectively.

40 patients (30.3%) were illiterate, while 90(68.2%) and 2(1.5%) had completed education till middle and matric or above respectively. Out of total, 48 (36.4%) patients were employed and 84 (63.6%) were unemployed. 43 patients (32.6%) had disease duration <1 year and 89 (67.4%) had disease for >1 year. 52 patients (39.4%) had mild disease, while 42(31.8%) and 38 (28.8%) had moderate and severe disease respectively (Table-1).

Table 1: *Demographic Data of Patients*

		No. of Patients (n = 132)	
		n	%
Age	16-25 years	65	49.2
	26-40 years	67	50.8
Socio-economic status	Low	43	32.6
	Middle	41	31.1
	High	48	36.3
Educational status	Illiterate	40	30.3
	Upto middle	90	68.2
	Matric or above	2	1.5
Employment status	Employed	48	36.4
	Unemployed	84	63.6
Duration of disease	<1 year	43	32.6
	>1 year	89	67.4
Severity of disease	Mild	52	39.4
	Moderate	42	31.8
	Severe	38	28.8
Effect of disease	No effect	1	0.7
	Mild effect	34	25.8
	Moderate effect	33	25.0
	Very Large effect	56	42.4
	Extremely Large effect	8	6.1



Mean DLQI score among hirsutism patients was 10.78 ± 5.99. Effect of disease on quality of life was noted as follows: No effect on 1 patient (0.7%), Small effect on 34 patients (25.8%), Moderate effect on 33 patients (25%), Very large effect on 55 patients (42.4%) and Extremely large effect on quality of life of 8 patients (6.1%) as seen in Pie chart 1. According to stratification of DLQI score with respect to different variables, high DLQI score was significantly associated with higher education, socioeconomic status and severe disease. No effect of age, employment status or duration of disease was noted.

Table 2: *Stratification of DLQI Score with Respect to Effect Modifiers*

		n	Mean DLQI	Std. Deviation	p-value
Age groups	16-25 years	65	10.91	5.44	0.811
	26-40 years	67	10.66	6.52	
Socio-economic status	Low	43	11.26	6.46	
	Middle	41	10.83	5.83	0.00002
	High	48	10.31	5.77	
Educational status	Illiterate	40	9.53	5.36	
	Upto middle	90	10.98	5.79	0.00001
	Matric or above	2	27.00	3.26	
Employment status	Employed	48	11.54	6.67	
	Not employed	84	10.35	5.56	0.074
Duration of disease	<1 year	43	10.60	5.63	
	>1 year	89	10.87	6.19	0.777
Severity of disease	Mild	52	6.56	3.06	
	Moderate	42	10.40	4.45	0.00002
	Severe	38	16.97	5.29	

Discussion

In our study, effect of disease on quality of life was noted as: No effect on one patient (0.7%), Small effect on 34 patients (25.8%), Moderate effect on 33 patients (25%), Very large effect on 55 patients (42.4%) and Extremely large effect on quality of life of 8 patients (6.1%). That means 65% patients had a DLQI score > 5 which indicates significant impact of the disease on quality of life. We found that mean DLQI score in our study population was 10.78±5.99. This was higher than that reported by Kutlu[3] who studied effect of hirsutism on quality of life of Turkish women. He reported no significant impact of severity of disease on quality of life which is contrary to our findings. This difference is probably because of smaller sample size and different ethnic background of their study population. Handjani et al[11] studied the impact of the disease on Iranian women and compared it before and after Laser hair removal. They reported a mean DLQI of 13.9 and significant reduction in this value after treatment.

Kiran et al.[12] reported a mean DLQI of 6.67±4.57 among Indian women suffering from hirsutism which is much lower than our observation. Furthermore, they didn't

report any significant role of any effect modifier which is also contrary to our observations. In a Swedish study by Ekbäck et al.[13] mean DLQI was reported to be 11.8 ± 8.4 which indicates significant impact of disease on quality of life. They too reported higher impact on psychosocial wellbeing with severer disease as we did. Behboodi et al.[14] too reported significant impairment of quality of life associated with PCOS related conditions including hirsutism, infertility and menstrual irregularities among Iranian women. Significant deterioration of psychological wellbeing was also highlighted by Alizadeh et al.[15] who reported a mean DLQI score of 7.75 ±2.36 among 200 Iranian hirsute women. This impact was significantly reduced after Laser hair removal. Gaber et al.[16] also highlighted the debilitation of everyday happiness caused by hirsutism among Egyptian women.

This marked negative effect on personality, daily activities, and interpersonal relationships suffered by hirsute women around the world was also highlighted by Mody.[17] There is dearth of local studies evaluating the effect of hirsutism on life of patients. In 2014, Baig et al.[18] reported a mean DLQI of 17.9±5.78 at Mayo hospital. This is much higher than our results. Probably over the years, advancement in management strategies have led to an overall improvement in disease related quality of life of these patients. Sidra et al. studied the patients of PCOS and reported that 87% of patients had poor quality of life due to hirsutism, which is quite alarming.[19]

Hirsutism is a common skin disease with many associated diseases and an unpredictable course which leads to a particularly huge dilemma especially races like ours where beauty and complexion have conventional standards and enormous psychosocial impact. This leads to social isolation of the patients. Therefore, while treating these patients their psychological wellbeing must be considered. Involvement of a psychologist and even a psychiatrist in special cases is inevitable. Hirsutism support group should be available and all hirsutism patients should be encouraged to join these groups.

Conclusion

Hirsutism has a significant impact on psychosocial life of patients as most patients reported moderate to extremely high negative impact on their lives. These effects can be markedly reversed by proper counselling, medical treatment, cosmetic measures and photo-epilation procedures. Therefore, clinicians must have an empathic attitude towards these patients and psychological aspects of disease should never be neglected.

Conflict of interest: *None*

References

1. Dorgham N, Sharobim A, Haggag H, El-Kalioby M, Dorgham D. Adding Combined Oral Contraceptives or Metformin to Laser Treatment in Polycystic Ovarian Syndrome Hirsute Patients. J Drugs Dermatol. 2021; 20(3):302-6.
2. Wankhade VH, Shah VH, Tomar SS, Singh RP. Clinical and Investigative Study of Hirsutism. J. clin. diagn. 2019;13(6): WC01-WC06
3. Kutlu Ö. Evaluation of quality of life of patients with hirsutism among Turkish women: A single-center cross-sectional study. J Cosmet Dermatol. 2020;19(11): 3053-7.
4. Finlay AY, Khan GK. Dermatology Life Quality Index (DLQI): a simple practical measure for routine clinical use. Clin Exp Dermatol 1994;19(3):210-6.
5. Belgaumkar VA, Chavan RB, Deshmukh NS, Warke NV. Impact of Vitiligo on Quality of Life: A Cross-sectional Pilot Study from Western India. J Skin Stem Cell. 2020;7(2):e107184.
6. Silpa-archa N, Pruksaeakanan C, Angkoolpakdeekul N, Chaiyabutr C, Kulthanan K, Ratta-apha W, Wongpraparut C. Relationship Between Depression and Quality of Life Among Vitiligo Patients: A Self-assessment Questionnaire-based Study. Clin Cosmet Investig Dermatol. 2020;13:511-20.
7. Chishti SH, Rafiq M. Psychosocial Issues, Coping Strategies and Psychological Symptoms of Hirsute Women. Pak J Med Sci. 2019; 58(3):141-8.
8. Lauritsen MP, Loft A, Pinborg A, la Cour Freiesleben N, Cohen A, Petersen JH, et al. Individualised gonadotrophin ovulation induction in women with normogonadotrophic anovulatory infertility: A prospective, observational study. Eur J Obstet Gynecol Reprod Biol 2017; 210:76-82.
9. Aswini R, Jayapalan S. Modified Ferriman-Gallwey Score in Hirsutism and its Association with Metabolic Syndrome. Int J Trichology. 2017;9(1):7-13.
10. Hongbo Y, Thomas CL, Harrison MA, Salek MS, Finlay AY J Invest Dermatol. 2005 Oct; 125(4):659-64.
11. Handjani F, Saki N, Kardeh B, Maghsoodi M. Assessment of laser therapy on the quality of life in patients

with hirsutism using the dermatology life quality index. Iran J Dermatol. 2013;16:6-8.

12. Kiran KC, Gupta A, Gupta M. The effect of hirsutism on the quality of life of Indian women. Int J Res Dermatol 2018;4:62-5.
13. Ekbäck M, Lindberg M, Benzein E, Årestedt K. Health-Related Quality of Life, Depression and Anxiety Correlate with the Degree of Hirsutism. Dermatology. 2013; 227:278-84.
14. Behboodi Moghadam Z, Fereidooni B, Saffari M et al. Polycystic ovary syndrome and its impact on Iranian women's quality of life: a population-based study. BMC Women's Health.2018;18:1-8.
15. Alizadeh N, Ayyoubi S, Naghipour M et al. Can laser treatment improve quality of life of hirsute women?. Int J Womens Health. 2017;9:777-80.
16. Gaber MA, El-Sayed SA. Quality of life in patients having hirsutism. Menoufia Med J. 2021;34:477-81.
17. Mody A, Shinkai K. Addressing important knowledge gaps about the disease burden of hirsutism. International Journal of Women's Dermatology. 2021;7(3):243-5.
18. Baig T, Aman S, Nadeem M, Kazmi AH. Quality of life in patients of hirsutism. J Pak Assoc Derma. 2014; 24 (3):217-23.
19. Sidra S, Tariq MH, Farrukh MJ, Mohsin M. Evaluation of clinical manifestations, health risks, and quality of life among women with polycystic ovary syndrome. PLoS One. 2019 Oct 11;14(10):0223329.

Authors Contribution

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

Efficacy of Excision with Tension-free Primary Closure for Sacrococcygeal Pilonidal Sinus: A single-center tertiary care experience

Jumana Fatima,[1] Muhammad Imran Anwar,[2] Muhammad Ali Rafique,[3] Muhammad Haris Janjua,[4] Muhammad Saqib Munir Rana,[5] Hassan Tariq[6]

Abstract

Objective: This study aims to evaluate the outcomes of simple excision and tension-free primary closure for sacrococcygeal pilonidal sinus.

Method: All the consecutive patients who underwent excision and primary closure for sacrococcygeal pilonidal sinus from February 2019 to May 2020 at Shaikh Zayed Hospital Lahore were studied retrospectively. Patients' demographics, operative details, postoperative complications, and recurrence were recorded and analyzed.

Results: A total of 50 patients (47 males and 3 females) were included in this study. The mean age and average BMI of the patients were 27.5 ± 6.36 years and 27.2 ± 1.76 kg/m2, respectively. VAS scores for postoperative pain were 6 ± 2.16, 2.5 ± 2.12, and 1.5 ± 0.70 on the 1st, 5th, and 10th postoperative days. Only 4 (8%) patients developed postoperative complications and the rest of the 46 (92%) patients recovered uneventfully. The overall success rate of excision with tension-free primary closure for PSD was 92%.

Conclusions: Complete excision with tension-free primary closure is a less invasive operative procedure for uncomplicated pilonidal sinus. It is associated with a higher rate of successful recovery, shorter hospital stays, and a low incidence of postoperative complications. Hence, the authors advocate this method as a preferred surgical option for the management of non-complex sacrococcygeal pilonidal sinus.

Keywords: Excision, Sacrococcygeal Pilonidal Sinus, Primary Closure, Hospital Stay, Post-Operative Complications, Recurrence

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Introduction

The pilonidal sinus is a fibrous tract lined by granulation tissue in the natal cleft, which often contains loose hair.[1] First described in 1883,[2] it mainly affects young adults with an incidence of 26:100,000 population.[3] It is predominantly seen in the age of 15 to 45 years,[4] being prevalent in males 2 to 4 times more than the females.[5] Formerly, the pilonidal disease was considered to be of congenital origin, but in current literature, it has been understood as an acquired condition caused by the retention of hair in the gluteal cleft.[3] Presence of hair in the intergluteal cleft induces an inflammatory reaction that leads to chronic infection, formation of abscess, and multiple sinus tracts or fistulas.[6]

Sacrococcygeal pilonidal sinus disease is linked with certain predisposing factors, which include deep natal cleft, trauma, excessive hair growth, high BMI, sweating,

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tight body wears, long sitting hours, and professions such as barbers or jeep drivers.[7] The affected people commonly present with the symptoms of discharge, pain, and swelling.[1] Besides physical discomfort, a troubled social life is among the major concern of the patients.

The treatment of choice for pilonidal disease is surgical management.[5] Surgical approach varies according to the patients' presentation and the surgeon's choice. The basic principle of surgery is the excision of all the sinus tracts to flatten the natal cleft, which is followed by healing of surgical wound with primary or secondary intention.[8]

Primary wound healing can be achieved either by midline suture closure or flap techniques e.g. V Y flaps and rotational flaps such as Limberg flap, modified Limberg flap (MLF), and gluteus maximus myocutaneous flap.[9] Singh A et al have affirmed that excision and primary midline closure is a safe procedure for uncomplicated pilonidal sinus with a mean operative time of 30 minutes, an average hospital stay of 1 day, return to normal activity within 8-14 days, and zero recurrences in a 6-month duration.[10] Despite the numerous surgical options, an optimal corrective operation for pilonidal sinus remains controversial.[3]

The objective of this study is to evaluate the outcomes of simple excision of the pilonidal sinus with tension-free primary midline closure in terms of duration of surgery, post-operative pain, hospital stay, postoperative complications, and recurrence. The results of this study will serve as an addition to the pre-existing literature as well as a guide for the management of this debilitating disease in our geographical area.

Material and Methods

This cross-sectional study was conducted from February 2019 to May 2020 at the Department of Surgery, Shaikh Zayed Hospital Lahore. All the patients of both genders, between 18-80 years of age with a history of pilonidal sinus for the last 1 year and who underwent excision and primary closure for pilonidal sinus under spinal anesthesia by a single surgical team in the same peri-operative settings were included in this study. Those with clinical and intraoperative findings of acute pilonidal abscesses as well as complex pilonidal sinuses (i.e. multiple fibrous tracts lined with granulation tissue or communicating with other organs), and those with documented ischemic cardiac conditions, coagulation disorders, and immunosuppressive states were excluded from the study.

A proforma was designed to collect all the data. Patients' demographic particulars (age, gender, addresses, and contact numbers), clinical signs and symptoms, dates of admission, operation, and discharge were noted in the proforma. Operative time, intra-operative findings, post-operative outcomes (i.e. VAS score for pain at 1st, 5th, and 10th postoperative day (POD), drain and suture removal days, postoperative complications, and duration of hospital stay), significant clinical findings on follow-up visits, and recurrence (if any) were also recorded.

All the patients took a post-operative five-day course of Ciprofloxacin (500mg × BD) and Metronidazole (400mg × TDS). All of them were advised to have bed rest for 1 week on their discharge letters. Patients were discharged with drains in situ and were recalled for follow-up at 5th and 10th POD for removal of drain and sutures, respectively. All the patients continued to be followed up for 12th months after the surgery.

The study was approved by the Institutional Review Board (IRB) of Shaikh Zayed Medical Complex, Lahore on 23rd December 2020.

Under spinal anesthesia, the patient was put in the Jack-Knife position to expose the inter-gluteal cleft. Both gluteus muscles were abducted by adhesive tapes attached to the sides of the operation table. Sinus openings were probed and hydrogen peroxide was injected through a feeding tube to delineate the main tract and its side branches if present. An elliptical incision was made around the sinus openings, all of the sinus tracts or cysts were excised and the dissection was continued down to the posterior sacral fascia. Bilateral skin and subcutaneous tissue edges were undermined to avoid closure of the defect under tension. Hemostasis was secured meticulously and a Redivac suction drain # 16 was placed in the wound bed. Interrupted tension sutures with Prolene-1 were laid and the wound was approximated by taking Prolene-1 mattress sutures through the skin, subcutaneous tissue, and posterior sacral fascia. Later on, tension sutures were tied over a gauze partially soaked with povidone-iodine and normal saline.

Statistical Package for the Social Sciences (SPSS) Ver. 20 was used for statistical analysis. Age, duration of symptoms, operative time, VAS scores, drain removal day, period of hospital stay, day of suture removal, and duration of return to normal activity were

described in mean ± standard deviation (SD). Data for gender, past history of pilonidal disease, post-operative complications (if any), and recurrence were expressed in terms of frequency and percentages.

Result

The present study included a total of 50 patients with PSD i.e. 47 (94%) males and 3 (6%) females. The mean age of the patients was 27.5 ± 6.36 years and the average BMI was 27.2 ± 1.76 kg/m2. In addition, a positive family history of pilonidal sinus disease was observed in 13 (26%) patients. (Table 1)

Table 1: *Patients' Characteristics and Course of Disease*

Total patients	50 (100%)
Males	47 (94%)
Females	3 (6%)
Mean age (years)	27.5 ± 6.36
Average BMI (kg/m^2)	27.2 ± 1.76
Positive Family History	13 (26%)
Past history of pilonidal surgery	5 (10%)
Mean duration of symptoms (months)	3.1 ± 0.42
Mean operative time (minutes)	32 ± 1.58

The mean VAS score for pain was 6 ± 2.16, 2.5 ± 2.12, and 1.5 ± 0.70 on the 1st, 5th, and 10th postoperative days, respectively. Patients were discharged in 1.5 ± 0.50 days

Table 2: *Post-Operative Outcomes*

Mean postoperative pain (VAS* Score)	1st POD	6 ± 2.16
	5th POD	2.5 ± 2.12
	10th POD	1.5 ± 0.70
Average hospital stay (days)		1.5 ± 0.50
Drain Removal (POD)		5 ± 1.41
Suture Removal (POD)		10 ± 2.82
Average return to normal activity (days)		11 ± 4.24
Postoperative Complications		4 (8%)
• Seroma		2 (4%)
• Hematoma		1 (2%)
• Wound infection		1 (2%)
Recurrence		0 (0%)

*VAS: Visual Analogue Scale

with drain. Drain and sutures were removed later on in the Outpatients Department. On average, patients reported a return to their normal activities in 11 ± 4.24 days post-operatively. (Table 2)

Postoperatively, 46 (92%) patients healed completely without any difficulty. However, 4 (8%) patients were affected by the postoperative complications. Amongst these four patients, two patients developed seroma after drain removal on the 5th POD that was treated conservatively with empirical antibiotics and anti-inflammatory agents. One patient suffered from hematoma formation on the 2nd POD due to blockage of the drain, which was managed by flushing the drain with saline. Additionally, one patient got his wound infected by Staphylococcus aureus requiring culture-specific antibiotic (Linezolid), the removal of alternate stitches for drainage, and wound healing by secondary intention. None of the patients reported any signs or symptoms of recurrence during the follow-up period of one year. (Table 2) Hence, the complication and recurrence rates recorded in our study were 8% and 0%, respectively. (Fig-1)

In our study, 46 out of 50 patients showed an uneventful recovery without any complication or recurrence up to a follow-up period of 12 months. Thus, the overall success rate of excision with tension-free primary closure for sacrococcygeal pilonidal sinus was 92%.

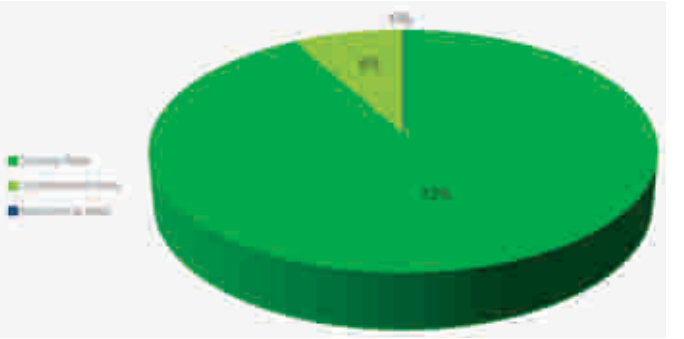

Fig-1: *Overall Success Rate of Excision with Tension-free Primary Closure for Sacrococcygeal Pilonidal Sinus*

Discussion

Pilonidal sinus is predominantly encountered before the 4th decade of life.[9] It affects the patients by posing significant physical discomfort, disturbed social life, and deterioration in the quality of life.[11] Management of pilonidal disease has evolved from conservative non-surgical to surgical techniques such as simple un-roofing, excision with primary closure, Z-plasty or advancement flaps, along with several minimally invasive therapeutic approaches e.g. pure phenol application, and laser

therapy.[12] Despite various management strategies, the standard treatment for PSD is still debatable among surgeons.[13]

The ideal management of the pilonidal disease should be less invasive ensuring rapid healing, shorter hospital stay, early return to normal life, decreased postoperative morbidity, and minimal recurrence.[13] Literature has revealed that excision with primary closure techniques is effective in attaining higher healing rates of 77 to 100%.[14]

In our study, the mean age was 27.5 ± 6.36 years, which can be attributed to the high sex hormone levels in young individuals.[15] Males, being more hirsute, are nearly 4 times more affected with PSD as compared to the women.[5] However, a significantly greater male-to-female ratio of 15.6:1 was observed in our study population. These results are quite relatable to another local study by Janjua MH et al[16] and can be ascribed to the socio-economic and cultural impediments that refrain the women of our geographical area to approach the hospitals. Moreover, the mean BMI of patients (i.e. 27. 2 ± 1.76 kg/m^2) in our study was above the normal values and around one-fourth (26%) of the patients had a positive family history, in concordance with the studies that described the body weight and family history as risk factors in the development of sacrococcygeal pilonidal sinus.[15, 17] However, our study has found no association of past surgery with the healing rate.The success of the surgical management for pilonidal disease lies in the complete removal of all the pilonidal sinus tracts. Alkata MA et al have observed a recovery rate of 78.2% after simple excision with tension-free closure of the pilonidal sinus.[13] Similarly, Singh A et al reported the efficacy of excision with primary closure for treatment of PSD in 37 out of 40 patients in his study.[10] In our study, a 1-year follow-up revealed a success rate of 92% with simple excision and primary midline closure, which is congruous with the earlier observations. These results can be accredited to the meticulous intra-operative dissection, tension-free primary midline closure, and diligent post-operative care by our surgical team.

Post-operative pain and patient discomfort are among the important factors that affect the choice of procedure for pilonidal disease. The VAS scores for pain at 1st, 5th, and 10th POD have shown minimal postoperative pain after excision with primary closure of pilonidal sinus and these scores are comparable to a study by Arnous M et al.[8] In our study, operative time, duration of hospitalization, and average return to normal activities of the patients was 32 ± 1.58 minutes, 1.5 ± 0.50 days, and 11 ± 4.24 days. These outcomes, being supported by several research works, establish the superiority of our technique over the other operative methods such as minimal excision and the Limberg flap procedure.[8,10,13,18]

Hematoma formation and sepsis are the main culprits that impair wound healing. The application of suction drainage systems is remarkably effective in the obviation of these complications.[19, 20] The rates of successful recovery and postoperative infection in our study favor the use of suction drain, which is also in line with previous research works.[20,21]

The recurrence rate is an imperative parameter to evaluate the efficacy of the surgical treatment for pilonidal sinus disease. The recurrence rates of excision with primary closure for PSD found in the published data ranged between 1 to 43%.[8,10] In our study, no recurrence has been recorded during the 12-month follow-up period. This zero recurrence is a notable finding, which augments the reliability and success of our surgical technique.

Excision and tension-free primary closure is a simple, safe, and cosmetically acceptable procedure as compared to excision with healing by secondary intention.[12] It also aims to minimize the duration of operation, post-operative pain, and average hospital stay, which are the inadequacies of reconstructive procedures.[8] Similarly, our study describes the efficacy of excision and primary closure for PSD in terms of less significant local wound complications, no re-admissions, and no reappearance of the symptoms.

Conclusion

Complete excision with tension-free primary closure is a simple, safe, reliable technique for the operative treatment of pilonidal sinus. It implies a greater percentage of successful recovery, low incidence of wound infection, shorter hospital stay, and early return to a normal routine with no recurrence of the disease. Based on these remarkable observations, the authors recommend the excision with primary closure as a preferred method for the treatment of pilonidal sinus.

References

1. Lunnis PJ. The anus and anal canal. In: Williams NS, O'Connell PR, MacCaskie AW eds. Bailey and Love's Short Practice of Surgery, 27th ed. Boca Raton: 2018: 1347-1349.

2. Velotti N, Manigrasso M, Di Lauro K, Araimo E, Calculli F, Vertaldi S, et al. Minimally invasive pilonidal sinus treatment: A narrative review. Open Med. 2019; 14: 532–536. DOI: 10.1515/med-2019-0059.
3. Sinnott CJ, Glickman LT. Limberg flap reconstruction for sacrococcygeal pilonidal sinus disease with and without acute abscess. Our experience and a review of the literature. Arch Plast Surg. 2019; 46(3):235-240.
4. Giuseppe F, Silivia DG, Patrizia R, Riccardo P, Antonio DS, Aldo RS, et al. Pilonidal sinus disease: Preliminary case-control study on heat wound dehiscence. Ann Med Surg 2019; 48; 144-149. DOI: 10.1016/ j.amsu. 2019. 07.032.
5. Alvandipour M, Zamani MS, Ghorbani M, Charati JY, Karami MY. Comparison of Limberg flap and karydakis flap surgery for the treatment of patients with pilonidal sinus diseases. Ann Coloproctol. 2019; 35(6):313-318.
6. Esposito C, Gargiulo F, Izzo S, Cerulo M, Del Conte F, Severino G, et al. Pediatric endoscopic pilonidal sinus treatment: An effective procedure for children with recurrent pilonidal sinus disease after failed open surgery. J laproendosc Adv Surg Tech A. 2019; 29(7): 981-986.
7. Hussein AA. The outcome of opened method versus closed method of chronic Pilonidal Sinus (PNS) at Baquba Teaching Hospital. Int. J. Adv. Res. Biol. Sci. 2018; 5(7):56-53.DOI:http:// dx.doi.org/10.22192/ ijarbs.2018.05.07.002
8. Arnous M, Elgendy H, Thabet W, Emile SH, Elbaz S A, Khafagy W, et al. Excision with primary midline closure compared with Limberg flap in the treatment of sacrococcygeal pilonidal disease: a randomised clinical trial. Ann R Coll Surg Engl. 2019; 101(1):21-29.
9. Sarhan AE, Sherif T, Zakaria Y. A prospective randomized trial comparing modified Limberg flap and cleft lift procedure in treatment of uncomplicated sacrococcygeal pilonidal disease. Egypt J Surg. 2016: 35(2): 89-95
10. Singh A, Kumar S, Jyoti V, Yadav P, Pandey A. Excision and primary closure of pilonidal sinus: excellent results. Int Surg J 2017; 4:3711-3.
11. Choy KT, Srinath H. Pilonidal disease practice points: An update. Aust J Gen Pract. 2019; 48(3):116-8.
12. Kober MM, Alapati U, Khachemoune A. Treatment options for pilonidal sinus. Cutis. 2018 Oct 1; 102(4): E23-9.
13. Alkatta MA, Mejally A. Excision and tension-free primary closure of pilonidal disease. Turk J Surg. 2019 Dec 16; 35(4):278-284. DOI: 10.5578/turkjsurg. 4368. PMID: 32551424; PMCID: PMC7282449.
14. Rogers P, Platell C, Levitt M. Minimal tissue excision in the treatment of pilonidal sinus disease: results from a single surgical unit. ANZ journal of surgery. 2020 Apr; 90(4):529-32.
15. Miller D, Harding K. Pilonidal sinus disease. World Wide Wounds. 2003 Dec. Available at: http:// www. worldwidewounds.com/2003/december/Miller/Pilonidal-Sinus.html
16. Janjua MH, Mohsin J, Fatima J, Siddique MU, Naseem MY, Gill AJ. Comparison of outcome of simple excision and primary closure with Limberg Flap procedure in Pilonidal disease. Isra Med J. 2021; 13(1): 11-14.
17. Manigrasso M, Velotti N, Fernandez LMS, Vertaldi S, Maione F, Gennarelli N, et al. Endoscopic Approach to Recurrent Pilonidal Sinus: A Retrospective Analysis. Journal of Laparoendoscopic & Advanced Surgical Techniques. 2021 Jan 1; 31(1):1-5.
18. Elgohary HG, Oraby EM. Pilonidal sinus: minimal excision and primary closure under local anesthesia. Egypt J Surg 2015;34:287-92
19. Kela M, Sharma R, Jain S. Our experience of simple technique for successful primary closure after excision of pilonidal sinus disease. International Surgery Journal. 2016 Dec 14; 2(4):647-51.
20. Iqbal MN, Asghar M, Waseem M, Bashir HM, Kousar N. Outcome of suction drain after excision of pilonidal sinus. JSZMC 2019;10(1): 1591-94
21. Tritapepe R, Padova DC. Excision and primary closure of pilonidal sinus using a drain for antiseptic wound flushing. Am J Surg. 2002; 183:209-11.

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JF, MIA: Data Collection
MHJ, MSMR: Literature Search
JF, MAR: Statistical Analysis
HT, MHJ: Drafting, Revision
MAR, HT: Writing of Manuscript

Association between Antiphospholipid Antibodies (APLA) and Preeclampsia (PE) in Females Presenting for Antenatal Check-up

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Abstract

Objective: To assess the association between antiphospholipid antibodies (APLA) and preeclampsia (PE) in females presenting for antenatal check-up.

Method: After ethical committee approval and informed consent 200 obstetric patients fulfilling inclusion criteria were included in this case control study from OPD of unit 2 Obstetrics and Gynecology Department of Lady Willingdon Hospital Lahore. Demographic record was maintained and two groups were created, case and control on the presence or absence of PE

Results: mean age of case group was 27.60±4.96 ranging from 20 to 35 years while mean age of control group was 27.94±4.13 also ranging from 20 to 35 years Mean gestational age of case group was27.46± 4.72 weeks ranging 20 to 35 weeks while mean gestational age of control group was 27.25± 4.74 weeks, ranging 20 to 35 weeks. There was significant association between preeclampsia and APLA as the p-value was significant (p-value=0.007).

Conclusion: Results of this study showed a significant association and significant risk between APLA and preeclampsia. obstetric patients with a high risk of preeclampsia, must have routine APLA assay.in women with early onset pre-eclampsia APLA should routinely be tested. When other clinical features are suggestive of APs.

Keywords: antiphospholipid antibodies (APLA), preeclampsia (PE), antenatal check-up

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Introduction

A group of antibodies called as Antiphospholipid antibodies (APLA) either binds to only cardiolipin or to a cofactor complexed cardiolipin or to a cofactor only. Incidence of APLA is about 5% in healthy people of the population. In low risk pregnant women prevalence of APLA ranges from 1-9%.[1] Antiphospholipid syndrome is an autoimmune condition characterized by a hypercoaguable state which causes many obstetric complications such as recurrent pregnancy loss, Intrauterine growth restriction, fetal demise and hypertensive disorders of pregnancy.[2,3] One third obstetric population with APS develops preeclampsia.[3,4]

APS was reported 27 years back in patients with systemic lupus erythematosus (SLE) and positive anticardiolipin antibodies manifesting with a clotting disorders of vessels. It was also observed that it caused poor obstetrical outcomes like pre-eclampsia. Literature does not support preeclampsia as a major criterion for diagnosis of APS, however it can be used as a minor criterion for APS diagnosis in patients having other APS manifestations.[4]

Study rationale is to determine the association of APLA with PE in obstetric population presenting in a tertiary care hospital for antenatal check-up. Literature has showed that there is significant association between APLA and PE but there are also contradictions present regarding association of APLA with PE. We planned

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this study to find whether there is any impact of APLA in the development of PE. Data is not available at local level and limited studies have been conducted in our setup. We aimed to conduct this study to find local magnitudes and can be able to detect increase in APLA in pregnant females in early gestational age and can prevent PE.

Material and Methods

This Case Control study was conducted in Unit II, Department of Obstetrics & Gynecology, Lady Willingdon Hospital, Lahore. The data collection technique was based on Non-probability consecutive sampling. The study sample size was 200. Both arms of study had 100 patients each (case and control) with 80% power of test and 5% level of significance and taking expected percentage of APLA i.e.10% in females having PE and 0% in females without PE. Patients between 20-35 years of any parity and singleton pregnancy of gestational age > 20 weeks of gestation on ultrasound were included. Cases were Females with PE (as per operational definition) and controls were females without pre-eclampsia. Females with chronic hypertension (Bp 140/90 mmHg) before pregnancy, chronic or gestational diabetes (BSR>200mg/dl), recurrent early pregnancy loss, history of autoimmune disease and deep vein thrombosis, depleted clotting factors, females using anticoagulants, females with infectious diseases (HIV inclusive) and malignancies (on medical record) and females on steroid therapy were excluded from the study. Hospital ethical committee approved the study. After informed consent 12 ml blood was taken from every patient of case (PE) and control group (without PE) presenting to OPD of Department of Obstetrics & Gynecology, Lady Willingdon Hospital, Lahore to assess presence or absence of APLA. All demographic data information (name, age, address, parity and gestational age) and study results were recorded on the proforma (attached). SPSS version 20 was used to analyze data. Mean ± SD was calculated for maternal age and gestational age. Frequency was measured for parity. Odds Ratio was calculated to measure relation between APLA and PE. OR>1 was taken statistically significant. Data was stratified for age and parity. Post stratification OR was calculated. OR>1 was considered significant.

Results

27.60±4.96 years was the mean maternal age of patients among case group, the minimum age was 20 years and maximum was 35 years whereas 27.94±4.13 was the mean maternal age of control group, the minimum age was 20 years and maximum was 35 years. (Table-1)

Table 1: *Descriptive statistics for age*

	Cases	Controls
N	**100**	**100**
Mean	27.60	27.94
Std. Deviation	4.96	4.139
Minimum	20	20
Maximum	35	35

Cases: Females with PE (as per operational definition)

Control: Females without PE presenting for antenatal routine checkup

The mean gestational age among cases was 27.46±4.72 weeks the minimum gestational age was 20 weeks and maximum was 35 weeks on the other side the mean gestational age among controls was 27.25± 4.74 weeks the minimum gestational age was 20 weeks the maximum was 35 weeks. Among cases there were 46 women whose parity was 1, 36 women's parity was 2 and 18 women's parity was 3 whereas among controls there were 28 women's whose parity was 1, 48 women's parity was 2 and 24 women's parity was 2.

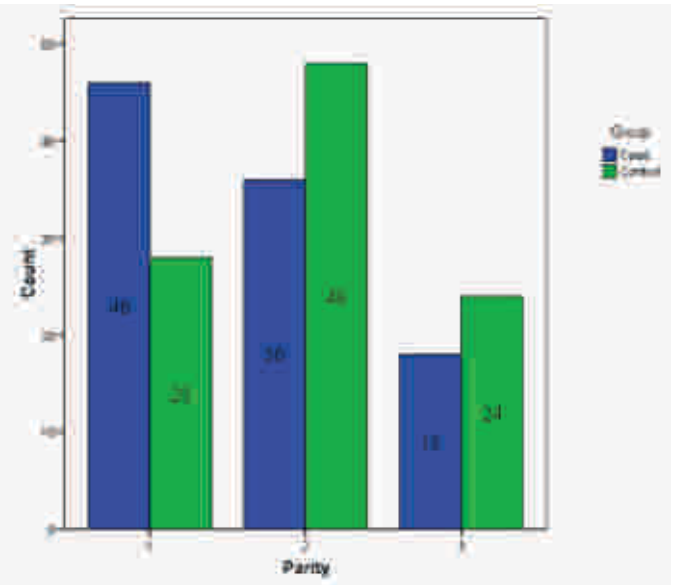

Fig-1: *Parity Status of Women*

Among cases there were 17 (17%) women in which Antiphospholipid antibodies were present where as in 83 (83%) APLA was absent, among controls there were 5(5%) women in which Antiphospholipid antibodies were present whereas among 95 (95%) APLA was absent. There was significant association between pre-

eclampsia and Antiphospholipid antibodies (APLA)

Table 2: *Association between APLA & preeclampsia*

		Group		Total
		Case	Control	
APLA	Present	17(17%)	5(5%)	22
	Absent	83(83%)	95(95%)	178
Total		100	100	200

as the p-value was significant (p-value=0.007). The odds ratio is 3.89 which means there are 3.89 time more odds of having preeclampsia if APLA is present in women. (OR=3.89)

There was significant association between APLA and preeclampsia in the age group of 20-28 years as the p-value was significant. (p-value= 0.041) there are 3.34 times more odds of developing preeclampsia in this age group if patient have APLA (OR=3.34) whereas in

Table 3: *Association between APLA and preeclampsia stratified for age groups*

		Age Groups			
		20-28 Years		29-36 Years	
		Case	Control	Case	Control
APLA	Present	12(%)	4(%)	5(%)	1(%)
	Absent	43(%)	48(%)	40(%)	47(%)
Total		55	52	45	48
Chi-Square Test		4.19		3.38	
p-value		0.041		0.066	
Odds Ratio		3.34		5.87	

Table 4: *Association between APLA & Preeclampsia Stratified for Parity*

		Parity					
		1		2		3	
		Case	Control	Case	Control	Case	Control
APLA	Present	11(%)	2(%)	3(%)	2(%)	3(%)	1(%)
	Absent	35(%)	26(%)	33(%)	46(%)	15(%)	23(%)
Total		46	28	36	48	18	24
Chi-Square Test		3.38		0.63		1.88	
p-value		0.066		0.24		0.17	
Odds Ratio		4.08		2.09		4.6	

the age group of 29-36 years there was no significant association between APLA and preeclampsia as the p-value was not significant (p-value=0.066) there are 5.87 times more Odds of developing preeclampsia is the APLA is present in patient.

There was no significant association between APLA and preeclampsia among the women whose parity was 1 but there were 4.08 times more odds of developing Preeclampsia among those women in which APLA was present whereas among women whose parity was 2 there was also no significant association between preeclampsia and APLA and there were 2.09 times more odds of developing preeclampsia if the APLA was present lastly women with parity 3 there was no significant association between Preeclampsia and APLA and there were 4.6 times more odds of developing pre-eclampsia if APLA was present.

Discussion

The results of our study indicate that patients presenting with preeclampsia tested positive for antiphospholipid antibodies more than those women without preeclampsia. Hypertensive disorders of pregnancy including preeclampsia are one of the major causes of maternal and perinatal morbidity and mortality. It is an estimation that preeclampsia complicates 2–8% of pregnancies[5,6] Patient manifests as having a high blood pressure, protein urea, lower limb edema and platelet aggregation.[5] It is a main cause of feto-maternal morbidity and mortality in developing countries.[7] Complication in pregnancies like recurrent early pregnancy losses are associated with the presence of APLA. Females with antiphospholipid syndrome have increased chance of developing preeclampsia, however the presence of APLA in preeclampsia is still not clear.[8] Devastating fetal and maternal complications like adverse fetal outcome, placental abruption, DIC and maternal mortality are linked to preeclampsia.[8] Above stated adverse events may not have APLA positivity. Literature associates APLA with miscarriages, intrauterine growth restriction, however there remains a controversy about their link with preeclampsia.[9-12] In a case control study in comparison to control that had 4.6% risk of complications in pregnancy, it increased to 59.1% in women with APLA particularly anti cardiolipin antibodies.[13,14] Benedict et al., found insignificant difference between preeclamptic and control females for presence of APLA i.e. 10% in preeclampsia group and 0% in control group.[15] Dreyfus reported no link between APLA and preeclampsia. The OR for the association was 0.95 (95% CI 0.45, 2.61). APLA were detected 4.4% (8/180) PE women and in 5.3% (19/360) controls.[16] However Roni Z, Mordechari D et al found that females with positive antiphospholipid antibodies were hospitalized earlier, had more complications including preeclampsia and gave birth at an earlier gestation.[17] The pathology of Pre-eclampsia and placental

insufficiency is multifactorial, but a proportion of cases are caused by antiphospholipid antibodies in maternal blood. Both case-control and cohort studies have reported associations between antiphospholipid antibodies and preeclampsia.[18]

In this study women who had preeclampsia among them 17(17%) were positive for APLA and among control only 5(5%) women were positive for APLA. However, a statistically significant association was seen between preeclampsia and APLA. i.e. (p-value=0.007) Women with preeclampsia had OR=3.89 hence more chances of having APLA positive in them.

Conclusion

Results of this study showed a significant association and significant risk between APLA and preeclampsia. Women at high risk for preeclampsia should be stratified for APLA assay. However, women with early severe preeclampsia and other features of APS must be considered for APLA testing.

References

1. Abou-Nassar K, Carrier M, Ramsay T, Rodger MA. The association between antiphospholipid antibodies and placenta mediated complications: a systematic review and meta-analysis. Thromb Res 2011; 128(1): 77-85.
2. Schreiber K, Radin M, Sciascia S. Current insights in obstetric antiphospholipid syndrome. Curr Opin Obstet Gynecol. 2017 Dec;29(6):397-403.
3. Roni Z, Micha B, Hades F. Early-onset preeclampsia – the impact of antiphospholipid antibodies on disease severity: a case-control study. Authorea sept 2020.
4. Ruiz-Irastorza G, Crowther M, Branch W, Khamashta MA. Antiphospholipid syndrome. The Lancet 2010; 376(9751):1498-509.
5. Benedict N, Augustina AO, Emefiele AM, Alexander NI. Antiphospholipid Antibodies in Women with Preeclampsia Seen at the University of Benin Teaching Hospital, Benin City, Nigeria. Int J Health Sci Res 2014;4(2):140-8.
6. ACOG Practice Bulletin No. 202. Gestational hypertension and preeclampsia. Obstet Gynecol 2019; 133(1): e1–e25.
7. Dreyfus M, Hedelin G, Kutnahorsky R, Lehmann M, Viville B, Langer B, et al. Antiphospholipid antibodies and preeclampsia: a case-control study. Obstet Gynecol 2001;97(1):29-34.
8. Laganà AS, Favilli A, Triolo O, Granese R, Gerli S. Early serum markers of pre-eclampsia: are we stepping forward? The Journal of Maternal-Fetal & Neonatal Medicine 2015:1-5.
9. Sibai BM. Diagnosis and management of gestational hypertension and preeclampsia. Obstetrics and gynecology 2003;102(1):181-92.
10. Ness RB, Roberts JM. Heterogeneous causes constituting the single syndrome of preeclampsia: a hypothesis and its implications. American journal of obstetrics and gynecology 1996;175(5):1365-70.
11. Vatten LJ, Skjærven R. Is pre-eclampsia more than one disease? BJOG: an International Journal of Obstetrics & Gynaecology 2004;111(4):298-302.
12. Villar J, Betran A, Gulmezoglu M. Epidemiological basis for the planning of maternal health services. WHO/RHR 2001;111:298-02.
13. Clark EA, Silver RM, Branch DW. Do antiphospholipid antibodies cause preeclampsia and HELLP syndrome? Curr Rheumatol Rep 2007;9(3):219-25.
14. Fischer-Betz R, Specker C, Brinks R, Schneider M. Pregnancy outcome in patients with antiphospholipid syndrome after cerebral ischaemic events: an observational study. Lupus 2012;21(11):1183-9.
15. Cohen D, Berger SP, Steup-Beekman GM, Bloemenkamp K, Bajema IM. Diagnosis and management of the antiphospholipid syndrome. Br Med J 2010; 340 (7756):1125-32.
16. Salehi R, Asl AA, Alizadeh M, Sayyahmelli M, Azarfarin R. Comparison of Antiphospholipid Antibodies in Hypertensive with Normotensive Pregnant Women. Rawal Med J 2007;32:173-5.
17. Roni Z, Mordechae D, Early-onset preeclampsia – The impact of antiphospholipid antibodies on disease severity European Journal of Obstetrics & Gynecology and Reproductive Biology (2021);263 :79–84
18. KJ Gibbins1 , AE Tebo2 , SK Nielsen, DW Branch Antiphospholipid antibodies in women with severe preeclampsia and placental insufficiency: a case-control study Lupus (2018) 0, 1–8

Authors Contribution

SM: Conceptualization of Project
MJ: Data Collection
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SP: Drafting, Revision
MH: Writing of Manuscript

Original Article

Effects of Flax Seed Oil on Histological & Biochemical Metamorphosis Induced by Caffeinated Energy Drink in Adult male Albino Rats Bone

Afifa Waseem,[1] Muhammad Suhail,[2] Alvia Batool,[3] Attya Zaheer,[4] Amna Rehman,[5] Ahmad Bilal Suhail[6]

Abstract

Objective: To appraise protective effects of flax seed oil on caffeinated energy drink induced histological (osteoporotic cavities) & biochemical (Alkaline phosphatase) changes in adult male albino rats bone

Method: This was an experimental study conducted at department of Anatomy Shaikh Zayed Postgraduate Medical Institute Lahore for 8 weeks. 32 adult male albino rats weighing (250-300gm) were randomly divided into four groups. Group A (Control) received corn oil 5ml/kg body weight in addition to basal diet daily for 8 weeks. Group B (Experimental) received caffeinated energy drink (15ml/kg body weight) and corn oil (5ml/kg body weight) for 8 weeks. Group C (Experimental) received caffeinated energy drink (15 ml/kg body weight) and 40% flax seed oil (5ml/kg body weight), while group D (Experimental) received caffeinated energy drink (15ml/kg body weight) and 60% flax seed oil (5ml/kg body weight) daily for 8 weeks respectively. All animals were weighed before and after experiment. Blood samples were taken before and after 24 hours of giving last doses for estimation of serum ALP. Furthermore, right femora were used for histological purpose.

Results: Significant difference in mean osteoporotic cavities of femora among experimental groups ($p = 0.000$) was observed. Insignificant difference was found in mean serum ALP ($p = 0.072$).

Conclusion: Flax seed oil helped in alleviating osteoporotic changes induced by caffeinated energy drink in femora of adult male albino rats.

Keywords: Flax seed oil, caffeinated energy drink, osteoporotic cavities, ALP

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Introduction

Caffeinated energy drinks are group of beverages tenanted our markets globally specially in younger population in order to amplify endurance performance.[1]

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They mainly contain caffeine as a stimulant drug in addition to taurine, glucose, sucrose, glucuronolactone, vitamin B1, B2, B6, B12, artificial flavor and sparkling water.[2]

Caffeine ($C_8H_{10}N_4O_2$) is the world's most widely used psycho active drug, chemically related to adenine and guanine bases of deoxyribonucleic acid (DNA) and ribonucleic acid (RNA).[3] It is naturally found is in coffee beans, guarana seeds and cocoa beans. Many caffeine based items like chocolate and its products, soft drinks, tea, coffee, ice cream, pain and flu medicines are commonly used in daily life.[4]

Caffeine acting as non-selective phosphodiesterase inhibitor raises intracellular CAMP, activates protein kinases-A, inhibits leukotrien synthesis and reduces

GABA production in tuberomamillary nucleus thus produces alertness.[5] Caffeine is metabolized in liver by P450 (CYP1A2) to active methylxanthine, theobromine and theophylline. It crosses blood brain barrier, placenta and can be found in breast milk.[6]

Long term use of caffeine not only leads to addiction and drug dependence but it increases risk of heart disease, type-2 diabetes mellitus, liver disease and bone resorption.[7] More than 300 mg a day can have deleterious effects on human body and its intoxication can lead to tachycardia, hypokalemia, gastrointestinal disturbances, hallucinations, seizures, arrhythmias and even death.[8]

Caffeine acting as a diuretic causes urinary excretion of calcium phosphorus and magnesium even after several hours of its intake.[9] It also hinders the absorption of vitamin D, essential for absorption of calcium from intestine. Various human studies revealed that young adults and women who consume adequate calcium and moderate caffeine may have little or no deleterious effects. However, adults and older women who used to take more caffeine than compensated loss of calcium are at higher risk of osteoporosis .[6,8,9]

The use of functional foods has also been increased universally not only due to their nutritional values but also secure against detrimental health problems.[10] Regarding this aspect flax seed and its various products have occupied a major proportion of ancient medical history along with documented positive effects on bone mass and their biomarkers.[10,11] Flax seed or linseed (Linum usitatissimum), has been cultivated for thousands of years by the ancient civilization of Ethopia and Egypt for textile fiber and nutrition. Flax seeds come from the flowers of plants and can be pressed into oil or ground into flax seed meal for baking.[12,13]

Flax seed oil is rich in Omega-3, Omega-6 fatty acids (ALA), Polyunsaturated fatty acids (PUFA), eicosapentanoic acid (EPA), docosahexaenoic acid (DHA), lignans, proteins, charbohydrates, Vitamin A, B1, B2, B6, C, E, folic acid and trace minerals like calcium, magnesium, phosphorus, potassium, copper, sodium and folate.[13] Omega-3 and Omega-6 fatty acids not only reduces inflammatory conditions like rheumatoid arthritis, osteoarthritis & osteoporosis but also provide protection against coronary artery disease, hypertension, hyperlipidemia, diabetes mellitus, chronic kidney disease (CKD), polycystic ovarian syndrome(PCOS) & metabolic syndrome.[13,14]

Taking into consideration the above mentioned beneficial effects of flax seed oil on human body and due to substantial use of caffeinated energy drinks in our youth, this study was designed to alleviate the hazardous effects of caffeinated drinks on osteoporosis and raised ALP levels of adult male albino rats.

Material and Methods

Thirty-two adult, healthy male albino rats, age (3-6 months), average weight (250-300 gm) were purchased from university of health science. They were divided into four groups. Group A (control), group B, C and D (experimental groups), each group consisting of 8 rats.

All the rats were kept at room temperature of 22±25 ℃. They were acclimatized for 7 days and had free access to food and water with ad libitum. A 12 hours light/ dark cycle was maintained.

After acclimitization, rats were divided randomly by lottery method into four groups. The weight of each rat was recorded before experiment and then marked with permanent markers for identification and placed in 4 different cages for 8 weeks.

Group A received corn oil 5ml/kg body weight by gavage for 8 weeks daily in addition to basal diet. Group B received 15ml/kg of caffeinated energy drink and corn oil 5ml/kg body weight daily for 8 weeks. Group C received 15ml/ kg of caffeinated energy drink and 40% flax seed oil (100ml oil formed by adding 40ml of flax seed oil and 60ml of corn oil) 5ml/kg body weight daily for 8 weeks. Group D received 15 ml/kg of caffeinated energy drink and 60% flax seed oil (100 ml oil formed by adding 60 ml of flax seed oil and 40ml of corn oil) 5ml/kg body weight daily for 8 weeks.[15]

After 8 weeks, all the rats were weighed individually, euthanized for dissection after 24 hrs of last doses. A vertical midline incision was given on each thigh of the rat. The skin was reflected and muscles were removed to view femora. Both right and left femora were dissected out, cleaned and weighed individually. Furthermore; right femora were selected for statistical purpose.

Tissue processing done according to Spencer and Bancroft procedure. Fixed right femora were cut into 3-5 mm small pieces from mid shaft and embedded in paraffin blocks.[16] 5µm thick sections were obtained and stained with haematoxylin and eosin. Slides of mid-shaft of femora were studied under light microscope by using various magnifications and comparison was made between control and experimental groups. Blood samples were taken from each animal via tail for estimation of serum ALP and then allowed to clot. The sera were immediately separated by centrifugation of the clotted blood and stored at -200C till analysis of biochemical

markers.[16]

Data was analyzed by using SPSS 20.0. The qualitative variable like osteoporotic cavities was reported by using frequency and percentage of each group. The quantitative variable like serum ALP was presented by using mean and standard deviation (S.D) and comparison among group was made by using One way ANOVA. Tukey's test for post hoc analysis was used where required. Chi-square test used for comparison among groups. Statistically significant p - value was ≤ 0.005

Results

Osteoporotic Cavities: Osteoporotic cavities in femora of all groups were observed. They were (100%) absent in group A (Fig. 1). (100%) present in femora of all rats of group B and the number of osteoporotic foci were more (5-6/field of vision) in this group (Fig. 2).

(25%) found in group C and their number were reduced (3-4/field of vision) (Fig.3). They were approximately (100%) absent in group D (Fig.4).

Figure.1 *Photomicrograph of longitudinal section of femur (mid shaft) group A, absence of osteoporotic cavities (H& E 10X)*

Figure. 2 *Photomicrograph of longitudinal section of femur (mid shaft) group B, presence of osteoporotic cavities (yellow arrow) along with disruption of normal architecture of bone tissue (H&E, 10X)*

Figure.3 *Longitudinal section of femur (mid shaft) group C, reduced no. of osteoporotic cavities (yellow*

arrow)(H&E, 10X)

Figure. 4 *Photomicrograph of longitudinal section of femur (mid shaft) group D, absence of osteoporotic*

cavities & restoration of normal architecture of bone. (H&E, 10X)

The difference among control and experimental groups was significant (p = 0.000) (Table 1)

Multiple comparisons of osteoporotic cavities among various groups by one way ANOVA showed significant difference between control group A and experimental group B, also between B, C and D, whereas insignificant difference was found between groups A, C & D (Table 2)

Table 1: *Osteoporotic cavities of femur of rats in control and experimental groups.*

Group	OSTEOPOROTIC CAVITIES		Total
	Present	Absent	
A	0 (0.0%)	8 (100.0%)	8 (100%)
B	8 (100.0%)	0 (0.0%)	8 (100%)
C	2 (25.0%)	6 (75.0%)	8 (100%)
D	0 (0.0%)	8 (100.0%)	8 (100%)
Total	10 (31.3%)	22 (68.8%)	32(100%)

p = 0.000* * Significant difference (p < 0.05)

Alkaline Phosphatase (ALP) (u/l):

The mean ALP (u/l) before and after the experiment in

Table 2: *Multiple comparisons of osteoporotic cavities of femur of rats in control and experimental groups.*

Group		Chi-square	DF	p-value
A	B	16.000	1	0.000*
	C	2.286	1	0.131+
	D	-	-	-
B	C	9.600	1	0.002*
	D	16.000	1	0.000*
C	D	2.286	1	0.131+

* Significant difference (p< 0.05)
\+ Insignificant difference (p > 0.05)
\- Constant Result

all groups were observed. One-way ANOVA test among groups showed insignificant difference in mean serum ALP (u/l) before and after experiment (p = 0.096 and 0.072) respectively. (Table 3)

While comparing various groups ALP (u/l) before and after experiment. ALP (u/l) in group B was higher

Table 3: *Alkaline phosphatase (u/l) in control and experimental groups*

	Group	Alkaline Phosphatase (u/l)	
		Mean± SD	p-value
Alkaline Phosphatase u/l before experiment	A	679.38 ± 172.27	0.096+
	B	539.75 ± 159.16	
	C	482.25 ± 154.54	
	D	529.88 ± 141.99	
Alkaline Phosphatase u/l after experiment	A	694.25 ± 174.39	0.072+
	B	639.88 ± 174.55	
	C	498.25 ± 160.58	
	D	523.88 ± 143.82	

\+ Insignificant difference (p> 0.05)

as compared to control group A, however insignificant difference was found in between them. There was also insignificant difference observed in between group C and D as compared to control group A.

Discussion

Caffeinated energy drinks have raised special health concerns in the recent past years due to deleterious effects on human body.[3,8] Public interest towards functional food has been developed due to potential health benefits of their ingredients. According to European commission, functional foods not only provide basic nutrition but also improve physical and mental health and decrease the risk of diseases.[12,13]

Flax seed and its various ingredients have potential health benefits due to their important ingredients like PUFA, MUFA, ALA in form of Omega-3, omega-6 fatty acids, Vit A, B, C, E, trace minerals like calcium, phosphorus, magnesium, potassium and copper.[12,13,14]

In this study the presence or absence of osteoporotic cavities in all four groups were observed. It was significant (p = 0.000) (table 1). Multiple comparison of presence of osteoporotic cavities among various groups showed significant difference between control group A and experimental group B (p=0.000), between group B and D (p = 0.000) respectively, while insignificant difference was found in between A, C and D (table 2). According to Omaima et al, oral doses of caffeine lead to urinary excretion of calcium, phosphorus and magnesium even after several hours of consumption. Secondly, it inter-feres with absorption of vitamin D necessary for absorption of calcium from intestine. Uncompensated losses of calcium would be a risk factor for the development of osteoporosis.[17]

Another possible reason of the presence of osteoporotic cavities in group B was due to caffeine consumption which besides causing urinary excretion of calcium, phosphorus and magnesium also stimulated glucocorticoid production which in turn reduced osteoblastic activity and calcium absorption in gastrointestinal tract.[9,18]

Treatment of group C and D with 40% and 60% of flax seed oil respectively helped in reduction of osteoporotic cavities due to antioxidant activity of flax seed oil which help to restore osteoporosis.[11,19] It was in agreement with the work of Watkins et al, who reported that dietary omega-3 and omega-6 PUFA not only lower PGE-2 production but also increase EPA and DHA through modulation of cytokines, thus decreased bone resorption and osteoporosis. An over production of PGE-2 would impair bone by reducing the activity of osteoblas.[19] Ilesanmi et al, had also clarified the pathogenesis of osteoporosis in postmenopausal women due to overpro-duction of cytokines lead to imbalance between bone formation and resorption.[20] Costa et al, observed that flax seed ALA content increased HDL cholesterol and decreased the concentration of cholesterol which increa-sed the differentiation of osteoblasts and decreased osteoclast bone resorption.[21]

In the present study the mean serum ALP before and after the experiment in all groups was also observed. There was insignificant difference in mean serum ALP before experiment among all group (p = 0.096), however

after the experiment it was also insignificant (p = 0.072) (table 3). Multiple comparison of serum ALP among groups also showed insignificant difference in between control and experimental groups. The increase in ALP in experimental group B was due to caffeinated drink.

It was in accordance with the work of Taiwo et al, who also observed raised ALP in male and female rabbits at day 14 and 21 after administration of caffeinated drink. He also elaborated the reason of raised ALP in experimental groups as compared to control was due to hepatic canalicular obstruction associated with inflammation and hepatocellular injury. [22]

The gradual reduction of ALP in group C and D was due to protective effect of flax seed oil in these groups. The results of present research work were in relevance with the work of Boulbarounet al, who not only observed improvement in micro architecture of bone but also in reduction of serum tarterase resistant acid phosphatase (TRAP) and Alkaline phosphatase (ALP)in adult female rats suffering from osteoporosis when treated with 10% flax seed and sesame seed oil.[23] Tariq et al also concluded in study that serum ALP could be used as an index of decrease in bone mineral density.[24]

Conclusion

Flax seed oil helped in mitigating caffeinated energy drink induced osteoporosis and raised serum ALP. It should be added in diet to minimize bone and mineral loss both in younger and elderly group.

Conflict of interest: None

References

1. Kelsey A. Vercammen, J. Wyatt Koma, Sara N. Bleich. Trends in Energy Drink Consumption Among U.S. Adolescents and Adults, 2003–2016. American Journal of Preventive Medicine , 2019; DOI: 10.1016/j.amepre. 2018.12.007
2. Kara R. "Energy drink". Encyclopedia Britannica, 31 May.2019; https://www.britannica.com/ topic/ energy-drink
3. The Caffeine from Wikipedia (free encyclopedia) 2014; http://en.wikipedia.org/wiki/Caffeine.
4. Caffeine drug bank. University of Alberta. 2013; 16(9). https://www.drug.bank.ca/drugs/ DB00201# Pharmacology
5. Ishak WW, Ugochukwu C, Bagot K, Khalili D, Zaky C. Energy drinks: psychological effects and impact on well-being and quality of life-a literature review. Innov-ClinNeurosci. 2012; 9:25-34.[PMC free article] [Pub Med] [Google Scholar]
6. Van Dam RM, Hu FB, Willett WC. Coffee, Caffeine and Health. N Engl J Med. 2020; 383(4):369-378 doi: 10: 1056/NEJMra 1816604. PMID 32706535.
7. Neves DBDJ, Caldas ED, Determination of caffeine and identification of undeclared substances in dietary supplements and caffeine dietary exposure assessment. Food and chemical toxicology: an international journal published for the British Industrial Biological Research Association. 2017 Jully.
8. Pietramgelo A. The effect of caffeine on your body. 28 sep 2018; healthline. Com/health/ caffeine- effects-on- body.
9. Stepharie E. Reuter, Haylay B. ScHutz, Michael B. Ward, Crystal L Grent, Gemna M. Peach, et al. The effect of high dose, short term caffeine intake on renal clearance of calcium, sodium and creatinine in healthy adults. Van Dam RM, Hu FB, Willett WC. Coffee, Caffeine and Health. N Engl J Med. 2020; 383(4): 369-378 doi:10:1056/NEJMra 1816604. PMID 32706535.
10. British journal of clinical pharmacology. 87(11). Nov 2021-4461-4466.https://doi.org/10.1111/ bcp. 148566.
11. Ankit G,Vivek S, Neelam U, Sandeep G, ManveshS. Flax and flaxseed oil: an ancient medicine & modern functional food. J Food Sci Technol. 2014;https:// www.ncbi.nim.nih.gov/pmc/articles/PMC4152533
12. Shen C.L, Yeh.J, Rasty M.C, Chyu DM, Dunn.Y. Liand Watkins B.A. Improvement of bone quality in gonad-intact middle aged male rats by long chain n-3 poly-unsaturated fatty acid.Tissue Int. 2007; 80:286-293
13. Iliiades C. What are the health benefits of flax seed and flax seed oil? University Health News 12 jan 2020. University healthnews.com/daily/nutrition/contro-versial –flax seed-benefits.
14. Chen F, Wang Y, Wang H. et al. Flaxseed oil ameliorated high-fat-diet-induced bone loss in rats by promoting osteoblastic function in rat primary osteoblasts. Nutr. Metab (Lond) 2019; https://doi.org/10.1186/s12986-019-0393-0
15. Wahba HM,Ibrahim TAA. Protective effect of flaxseed oil and vitamin E on potassium Bromate-induced oxi-dative stress in male rats.Int.J.Curr.Microbiol App. Sci. 2013;2(9);299-309.
16. Spencer LT and Bancorft JD. Tissue Processing. In Theory and Practice of Histological Techniques, 6th, Churchiill Livingstone Elsevier, Philadelphia, PA, USA. 2008; 83-92.
17. Omaima E M, Elamin Abdalla E L K, Gada Tag E A. The effect of caffeinated beverages on urinary excretion of minerals in females. Academic journal of life sciences.

2018;6(4):35-42. http://arpgweb.com/ ? ic= journal & journal=18&info=aims

18. Xu D, Zhang B, Liang G, Ping J, Kou H, Li X, Xiong J, Hu D, Chen L,Magdalou J, Wang H.Caffeine-induced activated glucocorticoid Metabolism in the hippocampus causes hypothalamic-pituitary-adrenal Axis inhibition infetal rats. Plos One. 2012; 7(9):e44497 https:// www.ncbi.nlm.nih.gov/pubmed/22970234
19. Watkins BA, Li Y and Seifert MF. Dietary ratio of n-6/n-3 PUFAS and docosahexaenoic acid:actions on bone mineral and serum biomarkers inovariectomized rats. J NutrBiochem. 2006;17:282-289
20. Ilesanmi-Oyelere B L, Schollum B, Sherlock M, Mc-Connell S, Mros, J Coad et al. Inflammatory markers and bone health in postmenopausal women: a cross sectional overview. Immun Ageing, July 10.2019; 16 (ID):p.15 PMCID:PMC 6621960 doi:10-1186/ s12979-019-0155-x
21. Costa CAS, et al. Effects of diet containing flaxseed flour (Linumusitatissimum) on body adiposity and bone health in young male rats. Food Funct. 2016;7:698-703
22. Taiwo, lyaniwura O, Adesokan, Abdulfatai A. Toxico-dynamic effects of red bull energy drink in a randomized controlled study on local strains of adult rabbits. Journal of Biology and Life Science. 2018; 9(1):2157-6076 https://doi.org/10.5296/jbls.v9il.12651
23. Boulbaround S, Mesfioui A, Arfaoui A, Ouichou A and EL Hessni A.Preventive effects of flax seed and sesame seed oil on bone loss in ovariectomized rats. PJBS. Biological Sciences. 2008;11:13;1696-1701. http:// www. pjbs.org
24. Tariq S, Tariq S, Pervaiz K Lone, Khaliq S. Alkaline phosphatase is a predictor of bone mineral density in postmenopausal females. Pakistan journal of medical sciences. Pak J Med Sci.2019 May- June; 35(3):749-753

Authors Contribution

MS: Conceptualization of Project
AB: Data Collection
AR: Literature Search
AZ: Statistical Analysis
AB: Drafting, Revision
AW: Writing of Manuscript

Non-contrast Computed Tomography Imaging Findings and Diagnosis Of Cerebral Venous Sinus Thrombosis

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Abstract

Objective: To ascertain the frequency of abnormal imaging in patients with symptomatic cerebral venous sinus thrombosis.

Method: This was a prospective, Cross-Sectional study done in the Department of Neurology, Mayo hospital, Lahore. The study was conducted after approval from the ethical review board. The study duration was 5 years. Patients with clinically suspected CVST from june 2016 to June 2021 were enrolled. A total of 177 patients with symptoms and signs suggestive of CVST on the initial evaluation, irrespective of age and gender, were involved in the study. Diagnosis of CVST was made clinically and on CT brain plain and was later confirmed with MRI Brain plain & contrast and MRV.

Results: Of the study sample of 177 patients, 36 (20.34%) patients were male and 141 (79.66%) were females. The mean duration of symptoms was 2.53±1.27 weeks. Cord sign was observed in 14(7.9%) patients, hemorrhagic infarct in 35(19.8%), and infarct with edema reported in 37(20.90%) patients.

Conclusion: CT brain plain is non-invasive and is the most sensitive and best modality in detecting cerebral venous sinus thrombosis. In our study infarct with edema (20.90%) was the most observed abnormality followed by hemorrhagic infarct (19.8%). We delineate in this study that non-enhanced CT brain (NECT) can be used as a first-line investigation in suspected cases of CVST.

Keywords: Cerebral venous sinus thrombosis (CVST), Non-contrast computed tomography (NCCT)

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Introduction

Cerebral venous sinus thrombosis (CVST) accounts for 0.5% to 1% of all stroke patients[1] and has a unpredictable presentation and clinical course. This is most common in the third decade of life with predominance in females and in younger age group.[2] Non-contrast enhanced CT (NCCT) brain is a commonly performed imaging method for the evaluation of patients with CVST.[1,2] Now, MRI combined with MRV is being considered the most sensitive imaging technique and has replaced invasive digital cerebral angiography as a gold standard imaging technique in CVST.[3,5] The imaging finding for the diagnosis of the CVST is divided into direct and indirect findings.[6] Direct findings that are observed on non-contrast CT are dense cord sign, dense dural sinuses, dense jugular vein and dense triangle and empty delta sign on post-contrast. Indirect findings of cerebral venous sinus thrombosis includes hemorrhagic infarcts, non-hemorrhagic infarcts, multifocal hemprhhages and diffuse cerebral edema.[2,3]

Non–contrast CT brain has shown high sensitivity and specificity in detection of intra-cerebral edema (93.7% and 98%) and hemorrhage (94.8% and 98.7% respectively) in literature. Moreover, Contrast-enhanced CT has a sensitivity of 75-100% and specificity of 81-100%.[6]

The aim of the this research was to determine the fre-

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quency of abnormal non- contrast CT brain in patients with cerebral venous thrombosis.

Material and Methods

This was a prospective, cross-sectional study carried out in the Neurology department of the King Edward Medical University, Mayo Hospital Lahore, from june 2016 to June 2021. The study duration was Five years. The research was approved by an institutional review board and ethical committee of the hospital. Written informed consent was taken from all patients registered in the research. Demographics and imaging findings were recorded on a pre-designed proforma. Patients presenting with symptoms & signs such as headache, seizures, limb weakness, diplopia, decreased vision, and papilledema were labeled as symptomtic cvst and were included in the study. Patients between the ages of 20-60 years were enrolled. NCCT was performed at presentation in all patients and was followed by an MRI brain and MRV for the confirmation of diagnosis. Imaging interpretation was done by experienced radiologist. Patients with abnormal cerebrospinal fluid cytology and biochemistry, history or clinical symptoms suggestive of an arterial stroke or NCCT showing arterial territory infarct or hemorrhage, hydrocephalus, infectious and imaging suggestive of tumor were excluded.

Data were entered and analyzed with SPSS version 22. Mean and the standard deviation was calculated for quantitative variables like age. Descriptive statistics like gender and abnormal findings on NCCT were calculated and presented as frequencies and percentages. The data were stratified for age, gender, duration of symptoms to control the effect modifiers. Data was also analysed for gender specific differences in imaging findings. Post-stratification chi-square test was used and a p-value less than 0.05 was taken as significant.

Results

In this study total of 177 patients were enrolled. The mean age was 28.45±4.13 years with minimum and maximum ages of 21 and 36 years respectively. 36 (20.34%) patients were male while 141(79.66%) patients were females. The male to female ratio was observed to be 0.25:1.

The study results depicted that the mean duration of symptoms was 2.53±1.27 weeks. Generally, no evidence of signs of venous thrombosis on NCCT was shown in 70(39.55%) cases and 107(60.45%) showed abnormal NCCT.(Fig-1)

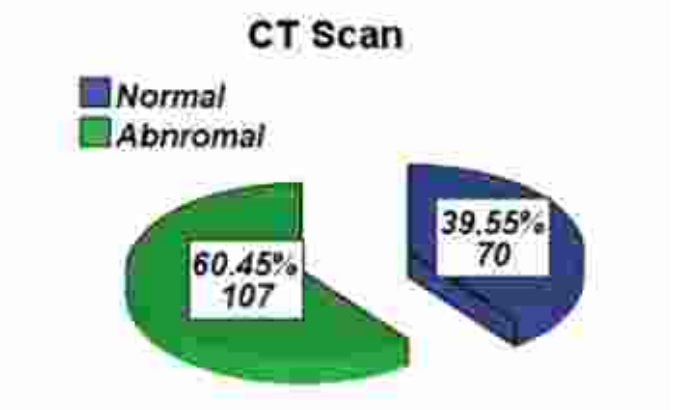

Figure:1 *Distribution of CT Scan Finding*

Among patients with age 30 years the normal NCCT was reported in 42(36.8%) patients (males 27.8% & females 42.6%). In subjects with age >30 years 28(44.4 %) had normal CT with p- value =0.322. For the duration of symptoms 3 weeks, the normal CT brain was reported in 63(47.0%) patients. However, patients who presented later than 3 weeks had abnormal findings on NCCT (16.3%, n=7). Significant relation between duration of symptoms and abnormal imaging was documented (p-value =<0.001).

Regarding abnormal NCCT, patients with age ≤30 years the abnormal NCCT was reported in 72 (63.2%) cases and with age >30 years 35(55.6%) cases had (P-value=0.322). The gender distribution of males and females is 72.2% and 57.4%, respectively.
Concerning the duration of symptoms ≤3 weeks, the 71(53.0%) had abnormal NCCT and with >3 weeks 36(83.7%) cases demonstrated abnormal NCCT imaging. (p-value= <0.001)

Table 1: *Comparison of CT scan findings with effect modifiers*

		CT Scan		Total	p-value
		Normal	Abnormal		
Age (years)	⩽30	42	72	114	0.322
		36.8%	63.2%	100.0%	
	>30	28	35	63	
		44.4%	55.6%	100.0%	
Gender	Male	10	26	36	0.106
		27.8%	72.2%	100.0%	
	Female	60	81	141	
		42.6%	57.4%	100.0%	
Duration of symptoms (weeks)	⩽3	63	71	134	<0.001
		47.0%	53.0%	100.0%	
	>3	7	36	43	
		16.3%	83.7%	100.0%	

Direct signs (cord sign) were observed in 7.9% (n=14) patients whereas indirect signs (hemorrhagic infarct

(n=35,19.85%) and infarct with edema (n=37, 20.90%). Besides cord sign in direct signs, hemorr-hage and infarct with edema in indirect signs, no other direct and indirect signs were noted in this study. Imaging findings according to age group, duration of symptoms, and gender distribution are outlined in Table 1 to Table 3.

Stratification of our data by age, gender distribution, and duration of symptoms demonstrates the following results. A relatively higher proportion of males exhibited abnormal non-contrast CT as compared with to female. Furthermore, this study showed a significantly increased prevalence of abnormal CT brain findings in patients who were less than 30 years compared to those who were more than 30 years old (p-value =0.003).

Regarding the duration of symptoms patients presented in acute phase (⩽ 3 weeks) were more likely to manifest evidence of thrombosis on imaging findings compared to cases who presented late (⩾3 weeks) (p-value= 0.001).

Table 2: *Comparison of hemorrhagic infarct with effect modifiers*

		Hemorrhagic infarct		Total	p-value
		Yes	No		
Age (years)	⩽30	28	86	114	0.031
		24.6%	75.4%	100.0%	
	>30	7	56	63	
		11.1%	88.9%	100.0%	
Gender	Male	9	27	36	0.378
		25.0%	75.0%	100.0%	
	Female	26	115	141	
		18.4%	81.6%	100.0%	
Duration of symptoms (weeks)	⩽3	21	113	134	0.016
		15.7%	84.3%	100.0%	
	>3	14	29	43	
		32.6%	67.4%	100.0%	

Table 3: *Comparison of infarct with edema with effect modifiers*

		Infarct with Edema		Total	p-value
		Yes	No		
Age (years)	⩽30	16	98	114	0.003
		14.0%	86.0%	100.0%	
	>30	21	42	63	
		33.3%	66.7%	100.0%	
Gender	Male	9	27	36	0.498
		25.0%	75.0%	100.0%	
	Female	28	113	141	
		19.9%	80.1%	100.0%	
Duration of symptoms (weeks)	⩽3	22	112	134	0.010
		16.4%	83.6%	100.0%	
	>3	15	28	43	
		34.9%	65.1%	100.0%	

Discussion

Cerebral venous sinus thrombosis has variable clinical presentation and therefore requires a high index of clinical suspicion. Clinical presentation can vary considerably based on the anatomical location and extension of thrombosis.[1] NCCT is a first-line modality to establish the proper diagnosis. Also commencement of early treatment translates to a better prognosis.

It has been seen in literature that CT scan conducted with detailed techniques that include plain and dynamic sequences and careful analysis of sources images is a simple and effective method to diagnose acute, subacute, and chronic venous thrombosis.[16] Initial NECT scan was done in all of our patients with symptomatic CVST, and diagnosis of venous thrombosis was later confirmed by MRV and MRI brain. In our study, 60.45% of patients had an abnormal finding on initial CT scan brain plain. In contrast, a study done by Jernej Avsenik et al[8] demonstrated 24.53% of the cases of CVST on initial NCCT.

Brain parenchymal abnormalities in cerebral venous thrombosis include diffuse cerebral edema, hemorrhage, and hemorrhagic infarct.[17,20,21]. A recent multicenter retrospective study demonstrated high sensitivity of 100% of hyperdensity on non-enhanced CT scans with specificity reaching 95%.[17] Another study presented that edema without hemorrhage is visualized on CT brain plain in ≈ 8% of cases and on MRI in 25% of cases.[18] And yet another study demonstrated that focal parenchymal changes with edema and hemorrhage may be identified in up to 40% of patients.[19] However, in our study hemorrhage on NCCT was demonstrated in 35.7 (19.8%) of patients, and infarct with edema was presented in 37 (20.90%).

NCCT is more likely to show evidence of thrombosis in the acute phase rather than in the chronic phase of venous thrombosis due to the signal changes of the clot with time on CT.[22] These results are in congruence with our research results which illustrates that patients who presented with symptomatic CVST early in their course in less three weeks had abnormal imaging com-

pared to who presented after the acute phase. In addition, in our study we also observed more abnormal finding in relatively younger age group of which no evidence was found in literature. Though this can be attributed to increased prevelance among younger age group.[20] Although, in our research there was notable prominence of abnormal imaging in males compared to females by 13%. Nevertheless, we did not found any evidence of this disposition in the literature. Because of diverse presentations in CVST, it must be put in the differential diagnosis in patients presenting with acute headache or other neurological complaints. Delay in recognition of CVST can lead to fatal consequences and worse outcomes and morbidity. Although, MRI with MRV is the imaging modality of choice. Despite that it is not readily available in every setup. Emergency NCCT brain should be performed to rule out the possibility of cerebral sinus thrombosis in symptomatic patients. Commencing heparin therapy on the day of presentation until a definitive diagnosis is made with MRI and MRV can potentially be lifesaving.

Conclusion

CT brain plain is a non-invasive and readily available neuro-imaging in emergency settings. It is highly sensitive in detecting the suspected cases of cerebral venous sinus thrombosis presenting in the emergency department. Moreover, our study illustrated the important differences between males and females in imaging findings.

References

1. Liang Z-W, Gao W-L, Feng L-M. Clinical characteristics and prognosis of cerebral venous thrombosis in Chinese women during pregnancy and puerperium. Scientific reports 2017; 7:43866.
2. Bousser M-G, Chiras J, Bories J, Castaigne P. Cerebral venous thrombosis--a review of 38 cases. Stroke 1985; 16(2):199-213.
3. Crawford SC, Digre KB, Palmer CA, Bell DA, Osborn AG. Thrombosis of the deep venous drainage of the brain in adults: analysis of seven cases with review of the literature. Archives of Neurology 1995; 52(11): 1101-8.
4. Karadas S, Milanlioglu A, Gönüllü H, Sayin R, Aydin MN. Cerebral venous sinus thrombosis presentation in emergency department in Van, Turkey. J Pak Med Assoc 2014;64(4):370-4
5. Vogl T, Bergman C, Villringer A, Einhäupl K, Lissner J, Felix R. Dural sinus thrombosis: value of venous MR angiography for diagnosis and follow-up. AJR American journal of roentgenology 1994; 162(5): 1191-8
6. James L. Leach, Robert B. Fortuna, Blaise V. Jones, Mary F. Gaskill-Shipley Imaging of Cerebral Venous Thrombosis: Current Techniques, Spectrum of Findings, and Diagnostic Pitfalls.Radiographics Vol. 26, No. suppl_1
7. Casey SO, Alberico RA, Patel M, Jimenez JM, Ozsvath RR, Maguire WM, Taylor ML. Cerebral CT venography. Radiology 1996; 198:163-170.)
8. Colin S. Poon1 2, Ja-Kwei Chang1, Amar Swarnkar1, Michele H. Johnson2 and John Wasenko1 Radiologic Diagnosis of Cerebral Venous Thrombosis: Pictorial Review. American Journal of Roentgenology. 2007; 189: S64-S75. 10.2214/AJR.07.7015
9. FreyJL, Muro GJ, McDougall CG, Dean BL, Jahnke HK. Cerebral venous thrombosis: combined intrathrombus rtPA and intravenous heparin. Stroke1999; 30: 489–494.
10. Benamer H, Bone I. Cerebral venous thrombosis: anticoagulants or thrombolyic therapy? : BMJ Publishing Group Ltd; 2000
11. Soleau SW, Schmidt R, Stevens S, Osborn A, MacDonald JD. Extensive experience with dural sinus thrombosis. Neurosurgery 2003;52(3):534-44.
12. Thrombosis in the young: epidemiology and risk factors. A focus on venous thrombosis. Rosendaal FRThromb Haemost. 1997 Jul; 78(1):1-6.)
13. The incidence of cerebral venous thrombosis: a cross-sectional study.Coutinho JM, Zuurbier SM, Aramideh M, Stam JStroke. 2012 Dec; 43(12):3375-7.)
14. Prateek Agarwal, Mahesh Kumar, Vipul Arora Clinical profile of cerebral venous sinus thrombosis and the role of imaging in its diagnosis in patients with presumed idiopathic intracranial hypertension. Indian J Ophthalmol 2010; 58:153-5
15. Dandy WE. Intracranial pressure without brain tumour-diagnosis and treatment. Ann Surg. 1937; 106: 492–513).
16. Teasdale E. Cerebral venous thrombosis: making the most of imaging. Journal of the Royal Society of Medicine 2000;93(5):234-7.
17. M. Garetier, J. Rousset, E. Pearson et al., "Value of spontaneous hyperdensity of cerebral venous thrombosis on helical CT," Acta Radiologica, vol. 55, no. 10, pp. 1245–1252, 2014.
18. Leach JL, Fortuna RB, Jones BV, Gaskill-Shipley MF. Imaging of cerebral venous thrombosis: current techniques, spectrum of findings, and diagnostic pitfalls. Radiographics 2006;26(suppl_1):S19-S41.

19. Mullins ME, Grant PE, Wang B, Gonzalez RG, Schaefer PW. Parenchymal abnormalities associated with cerebral venous sinus thrombosis: assessment with diffusion-weighted MR imaging. American journal of neuroradiology 2004;25(10):1666-75
20. Linn J, Pfefferkorn T, Ivanicova K, Müller-Schunk S, Hartz S, Wiesmann M, et al. Noncontrast CT in deep cerebral venous thrombosis and sinus thrombosis: comparison of its diagnostic value for both entities. American journal of neuroradiology 2009; 30(4): 728-35.
21. Cantu C, Barinagarrementeria F. Cerebral venous thrombosis associated with pregnancy and puerperium. Review of 67 cases. Stroke 1993;24(12):1880-4.
22. Digge P, Prakashini K, Bharath KV. Plain CT vs MR venography in acute cerebral venous sinus thrombosis: Triumphant dark horse. Indian J Radiol Imaging. 2018; 28(3):280-284. doi:10.4103/ijri.IJRI_328_17

Authors Contribution

SB, AN: Conceptualization of Project
MAJ, AN: Data Collection
MUF, UF: Literature Search
MAJ, AN: Drafting, Revision
AN, SB: Writing of Manuscript

Vaping and Associated Health Problems in University Students of Lahore

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Abstract

Objective: This study was carried out to assess health issues associated with Vaping among medical and non-medical students of Lahore.

Method: An analytical cross sectional study was conducted from March 2020 to July 2020 among students of multiple medical and non-medical colleges and universities. A sample of 160 students who were involved in vaping was collected through snow ball sampling technique. After IRB approval, pre-tested structured questionnaire was disseminated via Google forms. Students who were using E cigarettes and were willing to participate, were included in this study. Data was analyzed using SPSS version 22. Chi-square test was applied and p-value at <0.05 was considered significant to find out an association between knowledge and side effects reported in medical and non-medical students.

Results: This study included 160 students who were already involved in vaping, out of which 111(69.38%) were male and 49(30.63%) were female. Health effects associated include cough 38(27%), shortness of breath 24(15%), palpitations 18(11.25%) and loss of appetite 16(10%).When asked about different reasons behind starting e-cigarettes it was concluded as better alternative than smoking 70 (43.75%) followed by social up-gradation by 48 (30%) of the participants. Significant association was found among respondents using e-cigarettes and awareness regarding presence of nicotine (p=0.02), harmful chemicals (p=0.05) and adverse effects associated with it (p=0.002)

Conclusion: The study concluded that Vaping is more common in the students from other discipline rather than Medical students due to lack of information about its health hazards. Friends were the commonest source of information. Most of the non-medical students were unaware of harmful chemical ingredients present in e-cigarettes and the most common adverse effect reported was productive cough.

Keywords: vape, medical and non-medical students, health issues.

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Introduction

The industry of E-cigarettes has flourished in recent years with the ubiquity surpassing standard cigarette use among adults. Electronic cigarettes also known as electronic nicotine delivery systems (ENDS) which simulates tobacco smoking are battery-operated atomizers which delivers nicotine via inhalable aerosol generated from a nicotine-containing solution.[1] Other terms also used for this product includes "electronic cigarette," "e-cigarette," "e-cig," "e-pen," "e-hookah," "electronic hookah," "hookah pen," "hookah vape," "pen".[2] Recent statistics of WHO suggest that global market of E-cigarettes is increasing gradually accounting for 56 % by USA,12% by UK,21% is divided among China, France ,Germany, Italy and Poland.[3] The burgeoning of electronic Vaping products raises many solicitudes as they expose adolescents to different respiratory health issues, carcinogens and increasing nicotine dependence.[4]

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There is significant disparity in the prevalence of e-cigarettes from country to country. The prevalence of e-cigarettes usage in developed countries between years 2009-2013 is 7% in Australia, 6% in the U.S and 4% in the UK. In Asia, Malaysia has the highest prevalence of e-cigarette at 14% and Republic of Korea at 7% and notably China at 0.05%.[5] The prevalence in Bangladesh in 2018 was 0.4%, in India was 0.02% and in Pakistan the prevalence among adults is 7.1%.[6] There have been a multitude of studies carried out on the health impacts of e-cigarettes which included pulmonary ailments like upper and lower respiratory irritation, bronchitis, cough and emphysema.[7] In a study regular use of e-cigarette was linked to increased sympathetic control on the heart and oxidative stress, both related to increased cardiovascular disease risk.[8] Psychosocially e-cigarettes have shown an increase chance of development of depression, panic disorder, obsessive compulsive disorders, and alcohol drug use and abuse.[9]

Currently E-cigarettes are being promoted as a safer option to smoking traditional cigarettes or to facilitate quitting smoking completely.[10] E-cigarettes are commonly advertised to youth and young adults through television ads and can easily be bought online with little to none age verification making them easily accessible to even minors.[11] There is a ban on selling e-cigarettes in certain countries (Australia, Brazil, Canada, Mexico, Panama, Singapore, and Switzerland), and is regulated in 68 countries.[12] In Pakistan however, the import and sale of e-cigarettes is considered legal.[13] E-cigarettes are now an emerging public health concern across the globe. With an immense dearth of data and understanding of the prevalence, access, attitudes and awareness in the youth and young adults of developing countries, in-depth analysis of e-cigarettes are the need of the hour. Our study focuses on students of multiple medical colleges and non-medical institutes of Lahore and is aimed to assess the knowledge and health issues of students about the related health risk behavior specific to Vaping.

Material and Methods

This Analytical study was conducted through an online survey from March 2020 to July 2020. Google form having structured pre-tested questionnaire was generated for the purpose of data collection. Taking prevalence at 7.1 % similar to study conducted among university students in New Zealand in 2018,[14] confidence level of 95% and keeping the margin of error at 5%, a sample size of 377 was calculated through WHO online sample size calculator. Despite of large sample size, only 160 responses were obtained. Although Snow ball sampling technique was used for data collection to identify the students who were already vaping but due to social discrimination, many students ignored the request of primary investigator to fill in the google form. Students from different medical & non-medical colleges and universities were included in this study. Before collection of data, IRB clearance (Approval no M-19/043/-CM) was obtained from Institutional Review Board of Akhtar Saeed Medical and Dental College. Maintaining confidentiality, the collected data was reviewed, coded and entered in the Statistical Package for Social Sciences (SPSS) version 22. Variables were presented in the form of tables, bar charts and pie charts. Chi-square test was applied to find out association between knowledge of medical and non-medical students and associated side effects encountered in them and p value ≤ 0.05 was taken as significant association between dependent and independent variables.

Results

Total sample of the study was 160 students who were already involved in vaping, identified through snow ball sampling technique. Among these 160 students, 111(69.3%) were males and 49(30.63%) were females.

Table 1: *Socio-Demographic Profile (n=160).*

VARIABLES	FREQUENCY (n)	PERCENTAGE (%)
Age in Years		
16-20	46	28.75
21-24	111	69.3
More than 24	3	1.875
Gender Distribution		
Male	111	69.3%
Female	49	30.63
Course Of Study		
Medical students	59	36.88
Non-medical students	101	63.13
Father's Occupation		
Landlord	22	13.75
Office worker	13	8.13
Professional	87	54.38
Businessman	38	23.75
Monthly Family Income(Rs)		
Less than 30,000	19	11.8
30,000 – 70,000	59	36.95
More than 70,000	82	51.25

The respondent's mean age was 19±3.31 years. There was categorization of students according to age group and highest response was obtained from age group 21-24 years as this group included 111(69.3%) students. Out of total 160 students 59(36.88%) were Medical students and 101(63.13%) were from other discipline. Relating to the Father's income 82 (51.25%) were having monthly income of more than 70,000 rupees. (Table-1)

Table 2: *Knowledge and Awareness about E-cigarettes (n=160)*

Variables	Frequency (n)	Percentage (%)
Age since first use E-cigarettes		
12- 17 years	20	`12.52
18- 22 years	48	30.02
Above 22 years	92	57.5
Awareness regarding chemicals in E-cigarettes		
Yes	72	45
No	88	55
Chemical ingredient in E-cigarettes(n=72)		
Carcinogen	10	13.89
Nicotine	44	61.11
Tar	12	16.67
Lead	6	2.78
Frequency of E-cigarettes		
Daily	39	24.4
Weekly	7	4.4
Monthly	3	1.9
Occasionally	57	35.6
Source of knowledge about E-cigarettes		
Social & Electronic media	12	7.5
Magazines	1	0.6
Researches	2	1.2
Spouses	1	0.6
Advertisement	10	6.3
Family & Friends	85	52.5
Others	49	31.3
Knowledge about source of purchase of E-cigarettes		
Friend	20	12.5
Market	124	77.5
Online	16	10
Amount spent on E-cigarettes per month in Rupees		
Less than 10.000	54	33.75
10,000-14,000	75	46.8
More than 14,000	31	19.45
Reasons Behind Vaping		
Better alternative to smoking	11	9.4
Looks cool	10	8.1
Coping Stress	12	7.5
Trending among friends	30	18.8
Helps in quitting smoking	17	26.8
Enjoyable flavors	14	8.8
Relieve stress	12	7.5
To impress others	3	1.9
Others	51	37.3

Among total 160 students 92(57.5%) were using e-cigarettes above 22 years and 20(12.52%) students were those who were using e-cigarettes from 12 to 17 years. Regarding the awareness 72(45%) students out of total were aware of different chemicals present in E-cigarettes. Out of 72(45%) participants who were aware of chemicals, 44(61.1%) of them knew about nicotine in e-cigarettes, 12(16.67%) knew about tar, 10(13.89%) knew about carcinogen and 6(2.78%) knew about lead. (Table 2)

Out of total respondents, signs and symptoms experienced within 30 days or less after using vape was that 38 (27.5%) had cough 18(11.25%) experienced palpitations, allergies in 14(8.75%), chest pain in 18(11.25%), loss of appetite in 16 (10%), shortness of breath in 24 (15%) and wheezing 10 (6.25%) of the participants as illustrated in (Fig-1).

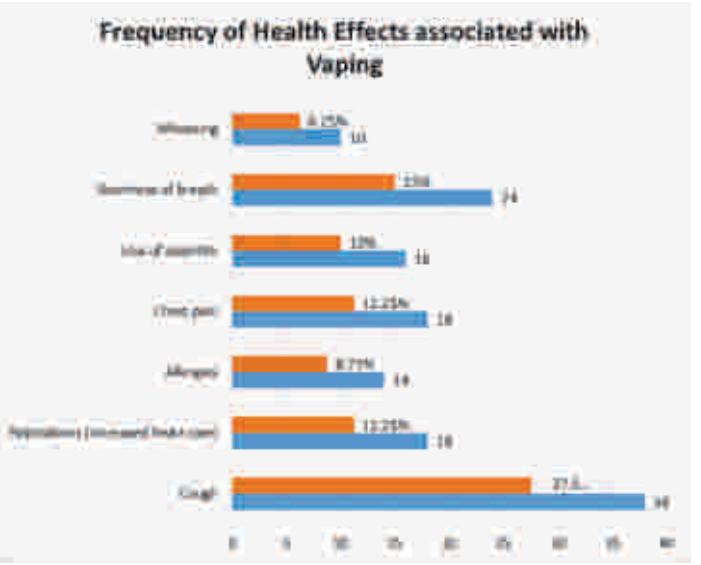

Fig-I: *Frequency of Health Effects Associated with Vaping*

Bi variate analysis was conducted to find out the difference in medical and non-medical students regarding knowledge, reason of vaping and side effects. It was observed that medical students had better knowledge about adverse effects related to E-cigarettes as compared to non-medical students. Majority of the medical students were aware that E cigarettes contain harmful

substances other than nicotine (p=0.05). Medical students had better knowledge that E cigarettes contain high level of nicotine (p=0.02). Lack of knowledge about ill health effects of vaping were observed in non-medical students. (Table 3).

Table 3: *Bivariate analysis about E-cigarettes awareness among medical and non-medical students.*

Variables	Medical students	Non-medical students	Total	p-value
E-cigarettes containing harmful substances beside Nicotine				
Not Aware	22(37%)	55(54%)	77(48%)	0.05*
Aware	37(62%)	46 (45%)	83(52)	
High Levels of nicotine in E-cigarettes				
Not aware	26(44%)	59(58.5%)	85(53%)	0.02*
Aware	33(56%)	42(41.5%)	75(47%)	
Awareness regarding adverse effects related to E-cigarettes				
Not aware	15(25%)	46(45%)	61(38%)	0.002*
Aware	44(75%)	55(55%)	99(62%)	
Money spent on E-cigarettes monthly				
Less than10,000	36(61%)	56(55.4%)	92(57.5%)	
Rs.10,000-12,000	18(30.5%)	34(33.8%)	52(32.5%)	0.592
More than 14,000	5(8.5%)	11(10.8%)	16(10%)	
Sources of knowledge about E-cigarettes				
Friends	30(50.8%)	50(49.5%)	80(50%)	0.468
Advertisement	5(8.47%)	5(4.95%)	10(6.45%)	
Family	2(3.5%)	2(1.98%)	4(2.5%)	
Magazines	0	1(0.99%)	1(0.625%)	
Researches	1(1.69%)	0	1(0.625%)	
Spouses	1(1.69%)	0	1(0.625%)	
Social media	3(5%)	9(8.25%)	12(7.5%)	
Others	17(28.8%)	34(33.6%)	51(31.8%)	
Reason behind purchasing E-cigarettes				
Better alternative than smoking	5(8.47%)	10(9.9%)	15(9.3%)	0.532
Presence of enjoyable flavors	6(10.16%)	8(7.92%)	14(8.75%)	
Helps in quitting smoking	8(13.5%)	6(5.94%)	14(8.75%)	
Trending among friends	7(11.8%)	23(22.7%)	30(18.7%)	
Relieve stress	6(10.16%)	6(5.94%)	12(7.5%)	
Looks cool	7(11.8%)	6(5.94)	13(8.125%)	
To impress others	0	3(2.97%)	3(1.87%)	
Others	20(33.89%)	39(38.6%)	59(36.8%)	

Discussion

Electronic nicotine delivery systems usage, which is referred commonly as e- cigarettes or Vaping has surged in popularity since its introduction in markets. Electronic cigarettes (e-cigarettes) and vape devices have rapidly become the most commonly used tobacco products by youth, driven in large part by marketing and advertising by e-cigarette companies.[15]

This research was carried out to see the frequency of Vaping, smoking and its related health issues in medical and non-medical students from other courses. Out of 160 respondents, 111(69.35%) were males and 49(30.63%) were females. However, in a similar study related to e- cigarettes usage carried out in Canada, 295(53.6%) were males and 256(46.4%) of the respondents were females.[16] In current study, the respondents of age group 21-24 years that is 111(69.3%) were the maximum number of the respondents, and was similar from the study conducted in United States of America where the age group with highest percentage of Vaping was also among 20-24 years old.[17] In this study, 59(36.88%) were medical students and 101(63.13%) students were from other courses of study. While a study conducted in Poland, 141(25.87%) were medical students and 195(37.28%) students were from other courses.[18] In our study, students from other fields of education were indulged more in Vaping and smoking than the students of medical universities which was due to ignorance about carcinogens and other harmful ingredients present in e-cigarettes and was similar to the research conducted in Poland in 2017 where the students of other courses used e-cigarette more than the medical students.[19] In this study, 39(24.38%) used e-cigarette daily, 10(6.24%) used e-cigarette weekly, and 111(69.38) used e-cigarette occasionally. In another study conducted in USA, 10.3% used e-cigarette daily, 59.5% used occasionally, 29.2% reported regular usage which was not similar to our study.[20]

In this study, 13(8.13%) of the respondents got information about e-cigarettes through Social & Electronic media, 11(6.8%) from advertisement and 136(85%) from family and friends. Similarly, in a qualitative study conducted in USA in 2020 showed friends was the most acceptable source of information.[21] Out of total participants, 20(12.5%) purchased e-cigarette from their friends, 124(77.5%) bought their e-cigarette from market and 16(10%) got their e-cigarette through online shopping platforms. Whereas an online study conducted in United States of America, 537 (31.1%) of their respondents purchased from a store or online, 282(16.3%) bought from friends and 259 (15%) from market and home deliveries.[22] In this regard our study was not similar to the study conducted in United States of

America where easy availability of e-cigarettes in markets along with online shopping stores with free home delivery has increased the usage of e-cigarettes among the students of different universities.

In our study, majority of participants thought that e-cigarettes are better alternative to smoking, while 30 (18.8%) used e-cigarette as a trend and 24(15%) used e-cigarette for coping with stress and depression. Similarly, in another survey conducted in the Germany, 2150 (85.6%) of the participants thought Vaping was helpful for cutting down on smoking while 430(14.4%) used for stress management.23 Out of 160 respondents, 84 (52.5%) were unaware of the chemicals/ingredients used in e-cigarettes whereas 72 (45%) were aware of the chemicals/ingredients used in e-cigarettes. Another study conducted in Flanders, where 53(70%) believed that e-cigarette contain chemicals which are carcinogenic, increase cardiovascular risk and increase the risk of lung disease.[24] The result indicated that highest percentage of students in this study did not know about the ingredients used in e-cigarettes.

In this study out of total respondents, signs and symptoms experienced within 30 days or less after using e-cigarette were, palpitations(increase heart rate) in 18(11.25%), allergies in 14(8.75%), chest pain in 18 (11.25%), loss of appetite in 16(10%), shortness of breath in 24(15%) and wheezing 10(6.25%),whereas in another study conducted in USA, symptoms experienced within 30 days were, chest pain 52(9.9%), shortness of breath 222(41.8%), wheezing 171(32.1%), chest tightness 119(22.5%), headache 234(44.1%) which were not similar to our study.25 Out of total respondents, 75 (46.875%) knew about different levels of nicotine in each cigarette and 85(53.125%) did not know about the levels of nicotine in e-cigarette. Similarly, another study conducted in United States of America, 146(28.5%) were using nicotine free e-liquid and 175(34.1%) were not knowing much about the e-liquid nicotine concentration.

Conclusion

The result of this study showed that students having less information and knowledge about harmful effects of E-cigarettes are more prone to Vaping. Male students were more involved than female students and friends were the commonest source of information about Vaping and e-cigarettes.

Conflict of Interest *None*

References

1. Hartmann-Boyce J, McRobbie H, Butler AR, Lindson N, Bullen C, Begh R, Theodoulou A, Notley C, Rigotti NA, Turner T, Fanshawe TR. Electronic cigarettes for smoking cessation. CDSR. 2021(9).
2. Andrei Shpakou A, Kovalevskiy V, Klimatskaia L, Naumau I, Sivakova S, Zaitseva O, et all. Traditional smoking and e-smoking among medical students and students-athletes–popularity and motivation. Family Med Prim Care. 2018;20(1):61-6.
3. Azagba S. E-cigarette use, dual use of e-cigarettes and tobacco cigarettes, and frequency of cannabis use among high school students. Addict Behav. 2018;79:166-70.
4. Rahman MA, Hann N, Wilson A, Worrall-Carter L. Electronic cigarettes: patterns of use, health effects, use in smoking cessation and regulatory issues. Tob Induc Dis. 2014;12(1):1-9. https:// link.springer. com/article/10.1186/1617-9625-12-21
5. Wagoner KG, Cornacchione J, Wiseman KD, Teal R, Moracco KE, Sutfin EL. E-cigarettes, hookah pens and vapes: adolescent and young adult perceptions of electronic nicotine delivery systems. Nicotine Tob Res. 2016;18(10):2006-12.
6. Dinakar C, O'Connor GT. The health effects of electronic cigarettes. NEJM. 2016;375(14):1372-81. https:// www.nejm.org/doi/full/10.1056/NEJMra1502466
7. Leventhal AM, Strong DR, Kirkpatrick MG, Unger JB, Sussman S, Riggs NR et al. Association of electronic cigarette use with initiation of combustible tobacco product smoking in early adolescence. JAMA. 2015; 314(7):700-7. DOI:10.1001/jama.2015.8950.
8. Giovenco DP, Hammond D, Corey CG, Ambrose BK, Delnevo CD. E-cigarette market trends in traditional US retail channels, 2012–2013. Nicotine Tob Res. 2014;17(10):1279-83.
9. Williams RS, Derrick J, Ribisl KM. Electronic cigarette sales to minors via the internet. JAMA Pediatr. 2015; 169 (3):1-6. DOI:10.1001/jamapediatrics.2015.63
10. Duke JC, Lee YO, Kim AE, Watson KA, Arnold KY. Exposure to electronic cigarette television advertisements among youth and young adults. Pediatr. 2014; 134(1):29-36.
11. Glantz SA, Bareham DW. E-cigarettes: use, effects on smoking, risks, and policy implications. Annu. Rev. Public Health. 2018;39:215-35.
12. Scheffler S, Dieken H, Krischenowski O, Förster C, Branscheid D, Aufderheide M. Evaluation of E-cigarette liquid vapor and mainstream cigarette smoke after direct exposure of primary human bronchial epithelial cells. Int J Environ Res Public Health. 2015; 12(4): 3915-25.

13. Vardavas CI, Anagnostopoulos N, Kougias M, Evangelopoulou V, Connolly GN, Behrakis PK. Short-term pulmonary effects of using an electronic cigarette: impact on respiratory flow resistance, impedance, and exhaled nitric oxide. Chest.2012;141(6):1400-6.
14. Wamamili B, Wallace-Bell M, Richardson A, Grace RC, Coope P. Associations of history of mental illness with smoking and vaping among university students aged 18–24 years in New Zealand: Results of a 2018 national cross-sectional survey. Addict. Behav. 2021 Jan 1; 112:106635.
15. Krause MJ, Townsend TG. Hazardous waste status of discarded electronic cigarettes. Waste Manag. 2015; 39:57-62.
16. Kennedy RD, Awopegba A, De León E, Cohen JE. Global approaches to regulating electronic cigarettes. Tob Control. 2017;26(4):440-5.
17. Jones SE, Kann L, Pechacek TF. Cigarettes smoked per day among high school students in the US, 1991–2009. Am J Prev Med. 2011;41(3):297-9.
18. Leavens EL, Stevens EM, Brett EI, Hébert ET, Villanti AC, Pearson JL et all. JUUL electronic cigarette use patterns, other tobacco product use, and reasons for use among ever users: results from a convenience sample. Addict Behav. 2019;95:178-83.
19. Brożek G, Jankowski M, Zejda J, Jarosińska A, Idzik A, Bańka P. E-smoking among students of medicine frequency, pattern and motivations. Adv Respir Med. 2017;85(1):8-14. DOI:10.5603/ARM.2017.0003.
20. Barnes AJ, Bono RS, Rudy AK, Hoetger C, Nicksic NE, Cobb CO. Effect of e-cigarette advertisement themes on hypothetical e-cigarette purchasing in price-responsive adolescents. Addiction. 2020;115(12):2357-68.
21. Dobbs PD, Clawson AH, Gowin M, Cheney MK. Where college students look for vaping information and what information they believe. J Am Coll Health. 2020; 68(4):347-56.
22. Wang TW, Gentzke AS, Creamer MR, Cullen KA, Holder-Hayes E, Sawdey MD, Anic GM, Portnoy DB, Hu S, Homa DM, Jamal A. Tobacco product use and associated factors among middle and high school students—United States, 2019. MMWR Surveill Summ. 2019; 68(12): 1.DOI:10.15585/mmwr. ss6812a1
23. Van Gucht D, Baeyens F. Health professionals in Flanders perceive the potential health risks of vaping as lower than those of smoking but do not recommend using e-cigarettes to their smoking patients. Harm Reduct. J. 2016;13(1):1-8.
24. Hefner KR, Sollazzo A, Mullaney S, Coker KL, Sofuoglu M. E-cigarettes, alcohol use, and mental health: Use and perceptions of e-cigarettes among college students, by alcohol use and mental health status. Addict Behav. 2019;91:12-20.
25. Ambrose BK, Rostron BL, Johnson SE, Portnoy DB, Apelberg BJ, Kaufman AR, et all. Perceptions of the relative harm of cigarettes and e-cigarettes among US youth. Am J Prev Med. 2014;47(2):S53-60.

Authors Contribution

SB: Conceptualization of Project
MJ: Data Collection
AI: Literature Search
MA: Statistical Analysis
SP: Drafting, Revision
MH: Writing of Manuscript

Metabolic Syndrome and Hyperandrogenemia in Polysystic Ovarian Syndrome

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Abstract

Objective: To ascertain the frequency of hyperandrogenemia in cases of polycystic ovarian syndrome and to correlate the frequency of metabolic syndrome in polycystic ovarian syndrome patients with and without hyperandrogenemia.

Method: This cross sectional study was conducted from 19.12.2020 to 18.06.2021 in Department of Obstetrics & gynecology, Unit-II, Aziz Bhatti Shaheed Teaching Hospital, Gujrat. Data was collected from a consecutive sample of 367 women diagnosed of polycystic ovarian syndrome(PCOS). All the female patients aged between 18-35 years diagnosed of PCOS included in the study except pregnant or lactating females.

Results: The mean age was calculated as 26.35 (± 5.28) years. Presence of hyperandrogenemia was found in 59.9% patients. In 220 hyperandrogenemic patients, the metabolic syndrome was present in 20% while metabolic syndrome was present in 10.20% patients without hyperandrogenemia. Significant higher occurrence of metabolic syndrome was found in hyperandrogenemia group as compared to without hyperandrogenemia group (20% VS 10.2%) having p-value = 0.014. Stratified age have significant relationship for the presence of hyperandrogenemia with p-value=0.000. Body mass index and duration of illness didn't show significant relationship having p-value > 0.05. Duration of illness was positively associated with presence of metabolic syndrome having p-value = 0.014.

Conclusion: Significant higher occurrence of metabolic syndrome was found in hyperandrogenemia group as compared to those without hyperandrogenemia in PCOS patients.

Keywords: Hyperandrogenism, Polycystic Ovarian Syndrome, Metabolic Derangement.

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Introduction

One of the most common female endocrinopathy is Polycystic ovarian syndrome (PCOS) affecting 8-12% of women in their reproductive age.[1] It is clinically characterized by irregular menstrual cycles, hyperandrogenemia, infertility, or sub-fertility, frequently with a characteristic ovarian morphology on ultrasound examination.[2] The pathogenesis of PCOS generally contains multiple pathways, ranging from insulin resistance, obesity, androgen hormone production and other environmental and lifestyle factors.[3]

Metabolic syndrome occurs in half of PCOS adults and one-third of PCOS adolescents,[4] and another study found it in 22.7% PCOS patients. An irregular gradation of insulin resistance is observed in about two-third PCOS cases; incidence of obesity is same, with reasonable variability amongst different populations.[5] In obese cases with PCOS, observations recommend that, metabolic aberrations associated to insulin resistance and obesity is in many cases, more vital in the mechanism of anovulation in PCOS than androgen excess.[3,4]

The most often investigated genes which play important role in pathogenesis of PCOS and related metabolic complications are CYP11, CYP17, SRD5A (steroid 5

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alpha reductase). They all cause increased production of testosterone and are also associated with insulin resistance. However, insulin resistance, HA and metabolic dysfunctions present from mild to severe degree in all patients depending on which gene is affected and thus insulin resistance and metabolic syndrome might be associated with hyperandrogenemia.[6,7]

Sung et al. (2014) reported that 60.7% of the PCOS patients had hyperandrogenemia and the frequency of metabolic syndrome was significantly higher among females with hyperandrogenemic PCOS (15.1% vs. 2.7%; $p<0.05$) as compared to women with non-hyperandrogenemic PCOS. In another study, Kim et al. (2014) reported the frequency of hyperandrogenemia to be 61.7% and also reported significantly higher frequency of metabolic syndrome in women with PCOS with hyperandrogenemia (19.7% vs. 11.9%; $p=0.008$) as compared to PCOS without hyperandrogenemia.[8-10]

However, Lerchbaum et al. (2014) in a similar study reported only insignificantly higher frequency of metabolic syndrome in PCOS women with hyperandrogenemia (9.4% vs. 4.3%; $p>0.05$) negating any such association. Yadav et al. (2014) also observed insignificant difference ($p>0.05$) in different metabolic derangements between Indian women with and without hyperandrogenemia.[10,11] There is a conflict of evidence (15.1% vs. 2.7%; $p<0.05$ 18, 19.7% vs. 11.9%; $p=0.008$ 19; 9.4% vs. 4.3%; $p>0.0520$) showing that hyperandrogenemic patient may have significantly higher frequency of metabolic syndrome. This conflict may be due to the variability of sample size, due to difference in the geno type (Korea vs. Germany vs India) or due to the difference in the geographical location of studies. Keeping in mind this conflict and the various factors that can lead to the different results and the higher mortality and morbidity associated with metabolic syndrome, there is a need to conduct such study in local population to correlate the occurrence of metabolic syndrome in respondents with and without hyperandrogenemia. The appropriate screening, timely identification and management can help in reducing the mortality and morbidity associated with metabolic syndrome.[12]

Material and Methods

This cross sectional study was conducted from 19.12. 2020 to 18.06.2021 in Department of Obstetrics & gynecology, Unit-II, Aziz Bhatti Shaheed Teaching Hospital, Gujrat. 367 women diagnosed with polycystic ovarian syndrome as consecutive sample, during the last 6 months presenting to outdoor of Obstetrics and Gynaecology were included. Ethical approval for study was taken from institutional review board (IRBA). After explaining the study, written informed permission was attained from all the patients. History and complete physical examination of these patients were taken to fill the questionnaire. Patients were requested to come with 12 hour fasting in the morning when under aseptic conditions venous blood samples were obtained. Serum total testosterone, free testosterone, glucose, high density lipoprotein, cholesterol and triglycerides were measured at the same day.

Presence of hyperandrogenemia was labelled when either total testosterone level ≥ 67 ng/dL or free testosterone ≥ 0.84 ng/dL. Metabolic syndrome was diagnosed when at least three of mentioned five metabolic abnormalities are present including, central obesity (waist circumference ≥ 80 cm), HDL (cholesterol ≤ 50 mg/dL), dyslipidemia (triglycerides ≥ 150 mg/dl), hypertension (BP $\geq 130/85$ mmHg), and hyperglycemia (fasting plasma glucose ≥ 100 mg/dl). Patient's demographic details along with presence/ absence of hyperandrogenemia and metabolic syndrome was observed and documented. To reduce bias, all the necessary investigations were attained from the same (hospital) lab. Confounding variables were excluded.

Women having Hyperprolactinemia (serum prolactin level ≥ 25.0 ng/ml), Hyperthyroidism (free T4≥ 1.8ng/dl) or hypothyroidism (free T4 ≤ 0.8ng/dl), Cushing's syndrome (24-hour urinary free cortisol $\geq 50\mu g/d$), Ovarian failure (follicle-stimulating hormone ≤ 0.3mIU/ml), Ischemic Heart Disease (as per history and clinical record of the patient) and pregnant (gestational amenorrhea, dating scan) or Lactating women (as per history from the mother) were excluded from the study.

All data was analysed through SPSS version 21. For quantitative variables like age, BMI and duration of illness mean and standard deviation was calculated. For qualitative variables like parity and presence of hyperandrogenemia and metabolic syndrome, frequency and percentages were calculated. Metabolic syndrome occurrence was correlated between patients with and without hyperandrogenemia by applying chi square test and considering $p \leq 0.05$ as statistically significant. Variables like age, BMI, parity and duration of illness were stratified to address effect modifiers. Post-stratifications chi-square test and independent sample t-test was used taking $p \leq 0.05$ as statistically significant.

Results

From 367 patients, it was observed that the mean age was 26.35 (± 5.28) years. The mean of body mass index was 26.12 (± 2.19) kg/m^2. The mean of duration of illness was 12.25 (± 4.06) months. There were 206 (56.1%) nulliparous patients and 161 (43.9%) multiparous patients. Presence of hyperandrogenemia was found in 220 (59.9%) patients while it was absent in 147 (40.1%) patients. The metabolic syndrome was present in 44 patients (20%) with hyperandrogenemia while metabolic syndrome was present in 15 (10.20%) patients without hyperandrogenemia. Presence of metabolic syndrome was significantly higher with hyperandrogenemia group as compared to without hyperandrogenemia group (20% vs 10.20%) having p-value = 0.014. By using independent sample t-test it was found that stratified age have significant relationship for the presence of hyperandrogenemia with p-value=0.000. Body mass index and duration of illness didn't show significant relationship having p-value > 0.05.

Table 1: *Presence of Hyperandrogenemia in Relation to Age, BMI and Duration of Illness.*

Variable	Mean±SD*	Presence of Metabolic Hyper-androgenemia		P-value
		Yes	No	
Age	26.35 ± 5.28	28.83±4.36	22.64±4.27	0.000**
BMI***	26.12 ± 2.19	26.07±2.23	26.20±2.16	0.560
Duration of Illness	12.25 ± 4.06	12.00±4.03	12.61±4.08	0.160

Standard Deviation, ** P-value < 0.05. * Body Mass Index*

Table 2: *Presence of Metabolic Syndrome in Relation to Age, BMI**, Duration of Illness and Hyperandrogenemia..*

Variable	Category	Presence of Metabolic Syndrome		P-value
		Yes N (%)	No N (%)	
Age	⩽25 years	7 (4.4)	153 (95.6)	0.000*
	> 25 years	52 (25.1)	155 (74.9)	
BMI**	⩽25	22 (15)	125 (85)	0.666
	> 25	37 (16.8)	183 (83.2)	
Duration of Illness	⩽1 year	38 (23.5)	124 (76.5)	0.001*
	> 1 year	21 (10.2)	184 (89.8)	
Presence of hyper-androgenemia	Yes	44 (20)	176 (80)	0.014*
	No	15 (10.2)	132 (89.8)	

** P-value < 0.05. ** Body Mass Index*

By using chi-square test it was found that metabolic syndrome occurrence was significantly associated with presence of hyperandrogenemia having p-value = 0.014. After stratification, significant association was found between age groups and presence of metabolic syndrome having p-value = 0.000. No Significant association was found between BMI and presence of metabolic syndrome with p-value = 0.666. Significant association was found between duration of illness and presence of metabolic syndrome having p-value = 0.014.

Discussion

This study was conducted to find out the frequency of hyperandrogenemia in patients presenting with polycystic ovarian syndrome and to correlate the metabolic syndrome occurrence in polycystic ovarian syndrome patients with and without hyperandrogenemia. Among 367 cases of PCOS, it was observed that the mean age was 26.35 (±5.28) years. The mean value of body mass index was 26.12 (± 2.19) kg/m^2. Hyperandrogenemia was found in 59.9% women whereas 40.1% women were normal. In a previous study conducted by Yadav G, et al., it was observed that from 200 PCOS women included in the study, 120 (60%) women were hyperandrogenic whereas the rest 80 (40%) women were normal.[11] The researcher further observed that majority of patients presented were in the age group of 21-30 years and the mean age was comparable between the hyperandrogenic and normoandrogenic groups. The BMI ranged from 15.5 to 45 kg/m^2, have no significant difference for the presence of hyperandrogenism (P= 0.950). Prevalence of hypertension (systolic BP [SBP] ≥ 135 mmHg and/or diastolic BP [DBP] ≥ 85 mmHg) was also comparable between the hyperandrogenic and normoandrogenic cases which is 9% versus 6% (P=0.396). Another research conducted by Majumdar et al. reported significantly higher prevalence of clinical hyperandrogenism (74.2% vs. 50.6%) in obese versus lean PCOS.[11,13]

In our study the mean of duration of illness was 12.25 (±4.06) months. The metabolic syndrome was present in 44 (20%) with hyperandrogenemia while metabolic syndrome was present in 15 (10.20%) patients without hyperandrogenemia. Presence of metabolic syndrome was significantly higher with hyperandrogenemia group as compared to without hyperandrogenemia group (20% vs 10.20%) having p-value = 0.014. By using independent sample t-test it was found that stratified age have significant difference for the presence of

hyperandrogenemia with p-value=0.000. Body mass index and duration of illness didn't show significant relationship having p-value > 0.05.[14] In premenopausal PCOS women, existing literature revealed that presence of hyperandrogenemia is highly associated with increased risk of metabolic syndrome. In another research conducted by Coviello et al., it was also found that hyperandrogenemia is a significant predictor of metabolic syndrome. They performed the research work on forty-nine adolescent females with PCOS.[15-18] In present research it was observed that presence of metabolic syndrome was significantly associated with presence of hyperandrogenemia having p-value = 0.014. After stratification, age groups and duration of illness was significantly associated with presence of metabolic syndrome having p-value=0.000 and 0.014 respectively whereas BMI have no significant association with presence of metabolic syndrome with p-value=0.667

Previous study showed that the prevalence of obesity was reported as 30–75% in women with PCOS.[19-21] It was found in another study conducted in Thailand that approximately 50% of PCOS subjects having BMI ≥ 25 kg/m^2.[15] In a multiracial group of women with PCOS, Mean BMI was reported higher than 32 kg/m^2 and proposed that there is strong association between obesity and PCOS.[15] But on the other hand after adjustment for age, the risk significantly increased among non-obese women with PCOS. However, after additional adjustment for BMI, this association was not statistically significant.[22,2]

Conclusion

Presence of hyperandrogenemia was found in 59.9% patients presenting with PCOS. Presence of metabolic syndrome was significantly higher with hyperandrogenemia group as compared to those without hyperandrogenemia.

Conflict of Interest: *None*

References

1. Shorakae S, Ranasinha S, Abell S, Lambert G, Lambert E, de Courten B, et al. Inter-related effects of insulin resistance, hyperandrogenism, sympathetic dysfunction and chronic inflammation in PCOS. Clin Endocrinol (Oxf) [Internet]. 2018 Nov 1 [cited 2022 Mar 13]; 89(5): 628–33. Available from: https://onlinelibrary. wiley. com/doi/full/10.1111/cen.13808
2. Ye W, Xie T, Song Y, Zhou L. The role of androgen and its related signals in PCOS. J Cell Mol Med [Internet]. 2021 Feb 1 [cited 2022 Mar 13];25(4):1825–37. Available from: https://onlinelibrary.wiley.com/doi/full/ 10.1111/jcmm.16205
3. González F, Considine R V., Abdelhadi OA, Acton AJ. Oxidative Stress in Response to Saturated Fat Ingestion Is Linked to Insulin Resistance and Hyperandrogenism in Polycystic Ovary Syndrome. J Clin Endocrinol Metab [Internet]. 2019 Nov 1 [cited 2022 Mar 13]; 104 (11):5360–71. Available from: https://academic.oup.com/ jcem/ article/ 104/11/5360/5530990
4. González F, Considine RV, Abdelhadi OA, Acton AJ. Hallmark evidence of lipopolysaccharide (LPS) tolerance in obese women with polycystic ovary syndrome (PCOS) - LPS-induced NFkB suppression in mononuclear cells (MNC) is linked to hyperandrogenism in PCOS. Fertil Steril [Internet]. 2018 Sep 1 [cited 2022 Mar 13];110(4):e8–9. Available from: http://www.fertstert.org/article/S0015028218306344/fulltext
5. Zeng X, Xie Y jie, Liu Y ting, Long S lian, Mo Z cheng. Polycystic ovarian syndrome: Correlation between hyperandrogenism, insulin resistance and obesity. Clin Chim Acta. 2020 Mar 1;502:214–21.
6. The association between Polycystic Ovary Syndrome (PCOS) and metabolic syndrome: a statistical modelling approach - Ranasinha - 2015 - Clinical Endocrinology - Wiley Online Library [Internet]. [cited 2022 Mar 13]. Available from: https://onlinelibrary.wiley.com/ doi/abs/10.1111/cen.12830
7. Ashraf S, Rasool SUA, Nabi M, Ganie MA, Jabeen F, Rashid F, et al. CYP17 gene polymorphic sequence variation is associated with hyperandrogenism in Kashmiri women with polycystic ovarian syndrome. https://doi.org/101080/0951359020201770724 [Internet]. 2020 [cited 2022 Mar 13];37(3):230–4. Available from: https://www.tandfonline.com/doi/abs/10.1080/09513590.2020.1770724
8. Abraham Gnanadass S, Divakar Prabhu Y, Valsala Gopalakrishnan A. Association of metabolic and inflammatory markers with polycystic ovarian syndrome (PCOS): an update. Arch Gynecol Obstet. 2021 Mar 1;303(3):631–43.
9. Saeed AA, Bahnassy AA, Al-Hamdan NA, Almudhaibery FS, Alyahya AZ. Perceived stress and associated factors among medical students. J Family Community Med [Internet]. 2016 [cited 2018 Jul 31]; 23(3): 166–71. Available from: http://www.ncbi.nlm.nih.gov/pubmed/ 27625584
10. Sanchez-Garrido MA, Tena-Sempere M. Metabolic dysfunction in polycystic ovary syndrome: Pathogenic role of androgen excess and potential therapeutic strategies. Mol Metab. 2020 May 1;35.

11. Yadav G, Radhakrishnan G, Gupta N, Madhu S. Comparison of metabolic parameters in hyperandrogenic and normoandrogenic women with polycystic ovarian syndrome. Fertil Sci Res [Internet]. 2014 [cited 2022 Mar 13];1(1):50. Available from: https:// www. fertility scienceresearch.org/article.asp?issn=2394-4285; year=2014;volume=1;issue=1;spage=50;epage=53; aulast=Yadav
12. Ashraf S, Nabi M, Rasool S ul A, Rashid F, Amin S. Hyperandrogenism in polycystic ovarian syndrome and role of CYP gene variants: a review. Egypt J Med Hum Genet [Internet]. 2019 Dec 1 [cited 2022 Mar 13]; 20(1):1–10. Available from: https:// link. springer.com/ articles/10.1186/s43042-019-0031-4
13. Majumdar A, Singh TA. Comparison of clinical features and health manifestations in lean vs. obese Indian women with polycystic ovarian syndrome. J Hum Reprod Sci [Internet]. 2009 Jan 1 [cited 2022 Mar 13]; 2(1):12. Available from: /pmc/articles/ PMC2700686/
14. Pateguana NB, Janes A. The contribution of hyperinsulinemia to the hyperandrogenism of polycystic ovary syndrome. J Insul Resist. 2019 Jul 2;4(1).
15. Weerakiet S, Srisombut C, Bunnag P, Sangtong S, Chuangsoongnoen N, Rojanasakul A. Prevalence of type 2 diabetes mellitus and impaired glucose tolerance in Asian women with polycystic ovary syndrome. Int J Gynecol Obstet. 2001 Nov 1;75(2):177–84.
16. Korhonen S, Hippeläinen M, Vanhala M, Heinonen S, Niskanen L. The androgenic sex hormone profile is an essential feature of metabolic syndrome in premenopausal women: a controlled community-based study. Fertil Steril. 2003 Jun 1;79(6):1327–34.
17. Apridonidze T, Essah PA, Iuorno MJ, Nestler JE. Prevalence and Characteristics of the Metabolic Syndrome in Women with Polycystic Ovary Syndrome. J Clin Endocrinol Metab [Internet]. 2005 Apr 1 [cited 2022 Mar 13];90(4):1929–35. Available from: https:// academic. oup.com/jcem/article/90/4/1929/2836532
18. Coviello AD, Legro RS, Dunaif A. Adolescent Girls with Polycystic Ovary Syndrome Have an Increased Risk of the Metabolic Syndrome Associated with Increasing Androgen Levels Independent of Obesity and Insulin Resistance. J Clin Endocrinol Metab [Internet]. 2006 Feb 1 [cited 2022 Mar 13];91(2):492–7. Available from: https://academic.oup.com/jcem/article/91/ 2/492/2843344
19. Ehrmann DA. Polycystic Ovary Syndrome. http:// dx.doi.org/101056/NEJMra041536 [Internet]. 2009 Oct 8 [cited 2022 Mar 13];352(12):1223–36. Available from: https://www.nejm.org/doi/full/10.1056/ NEJMra041536
20. Salley KES, Wickham EP, Cheang KI, Essah PA, Karjane NW, Nestler JE. POSITION STATEMENT: Glucose Intolerance in Polycystic Ovary Syndrome—A Position Statement of the Androgen Excess Society. J Clin Endocrinol Metab [Internet]. 2007 Dec 1 [cited 2022 Mar 13];92(12):4546–56. Available from: https:// academic.oup.com/jcem/article/92/12/4546/2596799
21. Abbott DH, Dumesic DA, Levine JE. Hyperandrogenic origins of polycystic ovary syndrome – implications for pathophysiology and therapy.https://doi.org/ 101080/ 1744665120191576522 [Internet]. 2019 Mar 4 [cited 2022 Mar 13];14(2):131–43. Available from: https:// www.tandfonline.com/doi/abs/10.1080/17446651.2019.1576522
22. Li S, Zhai J, Chu W, Geng X, Chen ZJ, Du Y. Altered circadian clock as a novel therapeutic target for constant darkness-induced insulin resistance and hyperandrogenism of polycystic ovary syndrome. Transl Res. 2020 May 1;219:13–29.

Authors Contribution

SSW, HH: Conceptualization of Project
HH, TN: Data Collection
HH, SSW: Literature Search
TN, HH: Statistical Analysis
TN, SSW: Drafting, Revision
HH, TN: Writing of Manuscript

Comparison of Efficacy of Cryotherapy Versus Intralesional Vitamin D3 in the Treatment Of Plantar Warts

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Abstract

Objective: To compare the efficacy of cryotherapy versus intralesional vitamin D3 in plantar warts.

Method: A Randomized controlled trial conducted from 30th July 2020 -29th January 2021 in the Department of Dermatology, Services Hospital, Lahore. 110 patients of both genders with age ranging from 18-60 years suffering from plantar warts (for more than 4 weeks) participated. Those allergic to xylocaine and Vitamin D3, pregnant females, immunocompromised, having bleeding disorders, Raynaud's phenomenon or cold urticaria were excluded. Participants were randomly divided in two groups. Group A patients was treated with cryotherapy and Group B was treated with intralesional Vitamin D3 for 4 sessions 2 weeks apart. Patients were followed at each treatment session every 2 weekly and then in OPD every month for 4 months for treatment response. Efficacy was assessed as complete cure of the lesion.

Results: Mean age of patients in group A was 34.36 ±12.06 years and in group B was 31.93 ±10.99 years with 81 (73.64%) patients between 18 to 40 years. Male patients were 76 (69.09%) and 34 (30.91%) were females. Efficacy of Group A was 56.36% while Group B showed 87.27% (p-value = 0.0001).

Conclusion: This study concluded that intralesional vitamin D3 is more effective than cryotherapy in the treatment of plantar warts.

Keywords: Plantar warts, intralesional vitamin D3, cryotherapy

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Introduction

Verrucae plantaris (plantar warts) are common cutaneous lesions of the plantar aspect of the foot that are caused by the human papillomavirus (HPV). There are more than 100 serotypes of HPV which cause different types of warts including common, plane, palmo-plantar, perianal and anogenital warts.[1] HPV virus is resistant to heat and drying, survives for longer periods at low temperatures and very contagious. Verruca vulgaris are the most common variety representing 70% of all cutaneous warts, common in school going children. Plantar warts, caused by HPV type 1, 2, 4 and 27, are hyperkeratotic papules having roughened surface and smooth collar of thickened horn occurring at pressure points of feet. In children may regress spontaneously but in adults become persistent.[2]

Plantar warts treatment depend on symptoms, patient preferences and cost.[1,2] Salicylic acid, cryotherapy, retinoic acid, podophyllin, topical 5-fluorouracil, Candida antigen, BCG, MMR vaccine interferon and imiquimod have been used for treatment but treatment failure and recurrence is common and treatment side effects are common cause of patient's dissatisfaction.[1] Therefore there has always been a quest for simple, safe and cost-effective treatment option in such patients.[2]

Cryotherapy freeze wart at -196°C leading to local inflammatory response.[2,3] It may result in hypopigmentation and pain.[1] Intralesional vitamin D3 upregulate vitamin D receptors resulting in production of antimicrobial peptides and cytokines thereby regulating cellular proliferation and differentiation. The most common side

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effect is pain at site of injection.[3,4]

Naresh et al.[3] (2019) reported the intralesional injection of vitamin D3 was associated with complete cure of lesion in 88.9% of Indian patients with plantar warts. In two other Indian studies, Singh et al. 4(2018) and Kavya et al.[5] (2017) reported the frequency of complete cure to be 72.5% and 82.6% respectively after intralesional injection of vitamin D3 while Aktaş et al.[6] (2016) reported it to be 80.0% in Turkish patients. While assessing the efficacy of cryotherapy, Tahir et al.[7] (2018) reported complete cure of lesion in 66.7% of Iraqi patients with plantar warts. Much lower frequency of complete cure has been observed by Bruggink et al.[8] (2015) and Cengiz et al.[9] (2016) who reported it to be 39.1% and 6.7% in Netherlands and Turkey respectively.

In the light of this review, intralesional vitamin D3 (72.5%[4] – 88.9%[3]) appears to be associated with higher frequency of complete cure than conventional practice of cryotherapy (6.7%[9] - 66.7%[7]) in patients with plantar warts. However, the evidence is currently limited to studies assessing the treatment response of these two treatment modalities individually and that can be biased due to differences in the population studied and skills of the treating dermatologist.

To the best of our knowledge, there is no single trial comparing these two therapeutic agents directly minimizing the selection bias. Therefore, we conducted this research to compare these two therapeutic options and the results will enable selection of more appropriate treatment option for patients with plantar warts in future practice.

Material and Methods

It was a randomized controlled trial conducted in the Department of Dermatology, Services Hospital, Lahore, 30th July 2020 to 29th January 2021. After approval from Hospital Ethical Review Board, total 110 patients (55 patients in each group) of either gender with age in the range of 18-60 years suffering from plantar warts (for more than 4 weeks) as per operational definition were enrolled through non-probability, consecutive sampling from outpatient department of dermatology. Plantar Warts: A single or cluster of skin lesions which is elevated, hard, rough, flesh-colored granular with pink base on clinical examination on plantar surface of foot mostly at pressure points of heel and metatarsal heads for more than 4 weeks. Patients suffering from warts in the preceding 6 months period only were included, after signing written informed consent to participate in the study. Patients who have taken any treatment during last four weeks, allergic to xylocaine or injection vitamin D, suffering from bleeding disorder (INR >2.0), having erythema around the wart or superadded infection were excluded. Pregnant and lactating mothers, patients with immunodeficient condition or taking immunosuppressive drugs, hypersensitive to cold such as Raynaud's phenomenon and cold urticaria, peripheral vascular disease, angina pectoris or other severe cardiac disease were also excluded.All the participants were than explained the details. Written informed consent and detailed history was taken from each patient along with measuring the size of lesions and photographs of lesions. These patients were then randomly divided into following two treatment groups using lottery method Group-A: Cryotherapy (n=55) in the group A, patients were treated with liquid nitrogen for 4 sessions 2 weeks apart. Liquid nitrogen was applied with cryogun in two freeze thaw cycles, each of 15 seconds duration, till freezing reaches 2 to 3 mm beyond the lesion in each thaw cycle. Group B: Intralesional vitamin D3 (N=55) in group B patients were treated with vitamin D, using aseptic technique 0.2ml of xylocaine plain 2% (20mg/ml) was injected by 30-gauge needle using insulin syringe at the base of the wart. Five minutes after injection the base of the wart was infiltrated with 0.6ml of vitamin-D3 200000 IU (Inj. Indrop-D 5mg/ml) by 30-gauge needle using insulin syringe. A maximum of 4 warts per session were injected at the base of wart. As in the group A, 4 sessions were delivered with a gap of 2 weeks. Patients were examined at each treatment session every 2 weeks for 2 months and then were followed in OPD every month for 4 months and to assess for treatment response. Efficacy was assessed as per operational definition. The efficacy was defined as ability of intralesional vitamin D3 or cryotherapy to result in complete clearance while moderate response is 50 to 99% resolution in size and number of lesions and mild response is 1 to 49% resolution in size and number of lesions. All the pre and post-treatment clinical examination was performed by a consultant dermatologist to eliminate bias. Confounding variables were controlled by exclusion. All the collected data were entered and analyzed through SPSS version 17. Numerical variables i.e., age, duration of disease and size of lesion at presentation were presented by mean ± SD. Categorical variables i.e. gender and efficacy were presented as frequency and percentage. Chi-square test was applied for comparison of efficacy between the groups taking p-value

≤0.05 as significant. Data were stratified for age, gender, duration of disease and size of lesion at presentation to address effect modifiers. Following stratification, chi-square test was re-applied for comparison of frequency of complete cure between the groups taking p-value ≤ 0.05 as significant.

Results

Age range in our study was from 18-60 years with mean age of 32.59 ±11.64 years. The mean age of patients in group A was 34.36 ±12.06 years and in group B was 31.93 ±10.99 years. Total 81 patients (73.64%) were between 18 to 40 years of age. Out of 110 patients, 76 (69.09%) were men and 34 (30.91%) were women with ratio of 2.2:1 as shown in figure I. Mean duration of disease was 7.77 ±2.54 weeks. Efficacy of Group A (Cryotherapy) was seen in 31 (56.36%) patients while in Group B (intralesional vitamin D3) was seen in 48 (87.27%) patients as shown in Figure II (p-value = 0.0001). Stratification of efficacy with respect to age groups and gender has shown in Table I & II respectively. Stratification of efficacy with respect to duration of disease shown in Table III.

Figure1: *Distribution of Patients according to Gender*

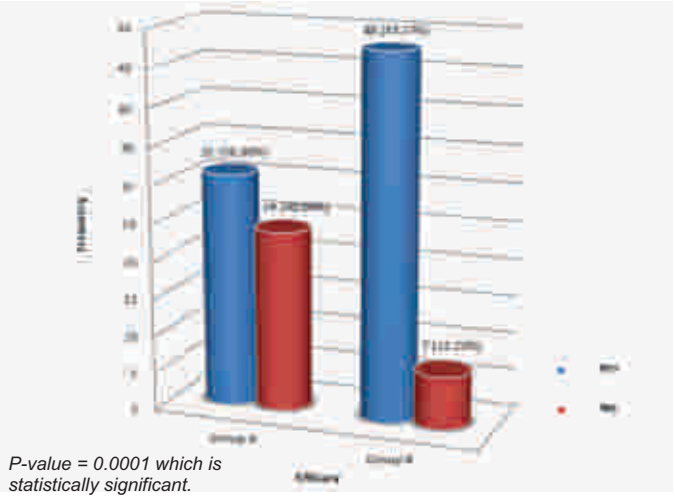

Figure II: *Comparison of the Efficacy of Cryotherapy Versus Intralesional Vitamin D3 in Plantar Warts*

Table 1: *Stratification of efficacy with respect to age groups*

Age of patients (years)	Group A (n=55)		Group B (n=55)		P-value
	Efficacy		Efficacy		
	yes	No	Yes	No	
18-40	23	18	33	07	**0.010**
41-60	08	06	15	00	**0.004**

Table 2: *Stratification of efficacy with respect to gender.*

Gender	Group A (n=55)		Group B (n=55)		P-value
	Efficacy		Efficacy		
	Yes	No	yes	No	
Male	24	13	36	03	**0.003**
Female	07	11	12	04	**0.034**

Table 2: *Stratification of efficacy with respect to gender.*

Duration of disease (weeks)	Group A (n=55)		Group B (n=55)		P-value
	Efficacy		Efficacy		
	Yes	No	yes	No	
≤8 weeks	19	16	36	03	**0.0001**
>8 weeks	12	08	12	04	**0.343**

Discussion

Warts are common cutaneous viral infections caused by the human papilloma virus (HPV), which has more than 100 strains; some of them are known to be premalignant. Warts occur more commonly in children and adolescents. May spontaneously disappear in a few but in majority persist and may spread to other body parts causing considerable physical and emotional distress.[10] Among treatment options are the conventional destructive and aggressive method, including chemical cautery, cryotherapy, electrocauterization, surgical excision, and laser ablation and non ablative is immunotherapy, which activates immune system to fight with the virus and suppress its activity. [11]

Topical vitamin D has been utilised in several studies for the treatment of common and anogenital warts. For example, Moscarelli et al[12] applied topical vitamin D in refractory warts in renal transplant patients. Rind et al[13] successfully used topical vitamin D in the clearance of anogenital wart in an infant. In both case reports, the effect of vitamin D on warts postulated to regulate epidermal cell proliferation and differentiation. In addition, Toll-like receptor activation of human macrophages upregulates the expression of VDR and vitamin D 1-hydroxylase genes, leading to release of antimicrobial peptides.[12,13] In a study of 17 patients with referatory warts, topical application of maxacalcitol ointment three times daily, cured warts within 2 weeks to 6

months.[14] Three immunocompromised patients with refractory warts were treated with topical vitamin D3 via a half-day occlusive dressing technique.[15]

This study is a comparison of cryotherapy versus intralesional vitamin D3 in the treatment of plantar warts. Mean patient age in our study cases was 32.59 ±11.64. Our study results have reported that majority of our study cases i.e., 81 (73.64%) belonged to age group of 18–40 years of age. Raghu Kumar et al[16] also reported viral warts being predominating 18–40 years age group which is similar to our study results. A study conducted by Moscarelli et al[12] reported 24.3 years mean age of the patients with warts which is less than our study results.

Out of these 110 patients, 76 (69.09%) were males and 34 (30.91%) were females with male to female ratio of 2.2:1. Such male gender preponderance has also been reported by Moscarelli et al[12] who reported 69% male gender predominance which is similar to our study results. While a study conducted Raghu Kumar et al[16] reported 56% female gender preponderance which is different from our study results. Mean duration of disease was 7.77 ±2.54 weeks. Raghu Kumar et al[16] and Moscarelli et al[12] reported very high duration of illness, the reason for this difference is due to our inclusion criteria as we only included warts having duration less than 3 months.

Efficacy of Group A (intralesional vitamin D3) was seen in 31 (56.36%) patients while in Group B (cryotherapy) was seen in 48 (87.27%) patients (p-value = 0.0001). Naresh et al.[3] (2019) reported the intralesional injection of vitamin D3 was associated with complete cure of lesion in 88.9% of Indian patients with plantar warts. In two other Indian studies, Singh et al.[4] (2018) and Kavya et al.[5] (2017) reported the frequency of complete cure to be 72.5% and 82.6% respectively after intralesional injection of vitamin D3 while Aktaş et al.[6] (2016) reported it to be 80.0% in Turkish such patients. While assessing the efficacy of cryotherapy, Tahir et al.[7] (2018) reported complete cure of lesion in 66.7% of Iraqi patients with plantar warts. Much lower frequency of complete cure has been observed by Bruggink et al.[8] (2015) and Cengiz et al.[9] (2016) who reported it to be 39.1% and 6.7% in Netherlands and Turkey respectively.

A trial done by Raghu Kumar et al, on 64 patients having warts showed that 90% of patients had complete clearance and 6.66% of the patients showed partial response when given intralesional vitamin D3.[16] Moscarelli et al applied topical vitamin D3 on referatory warts in renal transplant patients with good results.[17] Rind et al observed successful clearance of an anogenital wart in an infant after topically applying maxacalcitol.[18]

The vitamin D works through vitamin D receptors (VDRs) and vitamin D receptor activators (VDRAs) are immunomodulatory in function by regulating cell turnover. Toll-like receptor (TLR) activation of human macrophages upregulated expression of vitamin D receptor and vitamin D-1-hydroxylase genes resulting production of the antimicrobial peptide by infected cells as a part of innate immunity.[19] Isotretinoin when combined with calcitriol successfully cleared HPV-associated precancerous and cancerous skin lesions.[20]

Conclusion

The present study concluded that intralesional vitamin D3 can be used for treating plantar warts as its efficacy was higher than cryotherapy.

Conflict of interest: none

References

1. Vlahovic TC, Khan MT. The human papillomavirus and its role in plantar warts: a comprehensive review of diagnosis and management. Clin Podiatr Med Surg 2016;33(3):337-53.
2. Witchey DJ, Witchey NB, Roth-Kauffman MM, Kauffman MK. Plantar warts: epidemiology, pathophysiology, and clinical management. J Am Osteopath Assoc 2018; 118(2):92-105.
3. Naresh M. A study of effectiveness of intralesional vitamin D3 in treatment of multiple cutaneous warts. IOSR J Dent Med Sci 2019;18(3):84 -7.
4. Singh SK, Mohan A, Gupta AK, Pandey AK. A comparative study between intralesional PPD and vitamin D3 in treatment of viral warts. Int J Res Dermatol 2018; 4(2):197-201.
5. Kavya M, Shashikumar BM, Harish MR, Shweta BP. Safety and efficacy of intralesional vitamin D3 in cutaneous warts: an open uncontrolled trial. J Cutan Aesthet Surg. 2017;10:90-4.
6. Aktaş H, Ergin C, Demir B, Ekiz Ö. intralesional vitamin D injection may be an effective treatment option for warts. J Cutan Med Surg 2016;20(2):118 - 22.
7. Tahir NH, Sulaiman AA. Comparative study between cryotherapy and salicylic acid in the treatment of plantar warts in Erbil – Iraq. Zanco J Med Sci 2018;22(1):65-72.

8. Bruggink SC, Gussekloo J, Egberts PF, Bavinck JNB, de Waal MWM, Assendelft WJJ, et al. Monochloroacetic acid application is an effective alternative to cryotherapy for common and plantar warts in primary care: a randomized controlled trial. J Invest Dermatol 2015;135(5):1261-7.
9. Cengiz FP, Emiroglu N, Su O, Onsun N. Effectiveness and safety profile of 40% trichloroacetic acid and cryotherapy for plantar warts. J Dermatol 2016; 43(9): 1059-61.
10. Lynch MD, Cliffe J, Morris-Jones R. Management of cutaneous viral warts. BMJ 2014: 348:g3339.
11. Vender R, Bourcier M, Bhatia N, Lynde C. Therapeutic options for external genital warts. J Cutan Med Surg 2013; 17 Suppl 2 :61-7.
12. Moscarelli L, Annunziata F, Mjeshtri A, et al. Successful treatment of refractory wart with a topical activated vitamin D in a renal transplant recipient. Case Rep Transplant. 2011;2011:368623.
13. Rind T, Oiso N, Kawada A. Successful treatment of anogenital wart with a topical vitamin D(3) derivative in an infant. Case Rep Dermatol. 2010;2:46-9.
14. Imagawa I, Suzuki H. Successful treatment of refractory warts with topical vitamin D3 derivative (maxacalcitol, 1alpha, 25-dihydroxy-22-oxacalcitriol) in 17 patients. J Dermatol. 2007;34:264-6.
15. Egawa K, Ono T. Topical vitamin D3 derivatives for recalcitrant warts in three immunocompromised patients. Br J Dermatol. 2004;150:374-6.
16. Raghukumar S, Ravikumar BC, Vinay KN, Suresh MR, Aggarwal A,Yashovardhan DP, Intralesional Vitamin D3 injection in treatment of recalcitrant warts: a novel proposition. J Cutan Med Surg. 2017;21(4):320-4.
17. Moscarelli L, Annunziata F, Mjeshtri A. Successful treatment of refractory wart with a topical activated vitamin D in a renal transplant recipient. Case Rep Transplant. 2011;2011:368623.
18. Rind T, Oiso N, Kawada A. Successful treatment of anogenital wart with a topical vitamin D(3) derivative in an infant. Case Rep Dermatol. 2010;2:46-9.
19. Liu PT, Stenger S, Li H. Toll-like receptor triggering of a vitamin D- mediated human antimicrobial response Sci. 2006;311:1770–3.
20. Majewski S, Skopinska M, Bollag W, Jablonska S. Combination of isotretinoin and calcitriol for precancerous and cancerous skin lesions. The Lancet. 1994;344: 1510 –11.

Authors Contribution

HA, SA: Conceptualization of Project
HA: Data Collection
SD, AC : Literature Search
SS: Drafting, Revision
HE: Writing of Manuscript

Nephroprotective Effects of Ethanolic Extracts of Azadirachta Indica Seeds and Leaves in Diabetic Rats

Tahira Saleem, Abida Saleem, Nusrat Jabeen, Naila Saleem, Naima Khalid, Omaila Ikram

Abstract

Objective: To evaluate and compare the outcomes of effects of Azadirachta indica on serum urea and creatinine in alloxan induced diabetic albino rats.

Method: The study was a randomized controlled trail carried out in Physiology department of services institute of medi-cal sciences, Lahore from November 2018 to April 2019. 120 male albino rats were randomly and uniformly divided in four groups (n=30). Diabetic control and experimental groups were administered with alloxan monohydrate intraperitoneal injection of (120mg/kg) to induce diabetes mellitus. G1 (control) received normal saline orally; G2 was (diabetic control), group 3 received Neem leaves extract (500 mg/kg body weight); and group 4 received Neem seeds extract (500 mg/kg body weight) as a single dose for four weeks. Subsequently blood samples (4-5ml intracardiac) were collected from each group member on 29th day to evaluate the biochemical parameters of serum urea and creatinine.

Results: The ethanol based extracts of Neem seeds and leaves lead to highly significant ($p<0.001$) reduction in urea and creatinine levels of G3 and G4.

Conclusion: Azadirachta indica leaves and seeds can significantly contribute in lowering serum urea and creatinine

Key words: Azaditachta Indica, urea and creatinine lowering Effect.

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Introduction

The prevalence of diabetes mellitus is predicted to rise globally from an estimated 382 millions in 2013 to 592 million by 2035.[1] Type 2 diabetes has already attained epidemic level, while incidence of type1 diabetes is also increasing. It initially emerges as group of disorders with a defective or deficient insulin secretory process, glucose underutilization leading to hyperglycemia.[2] Patients with diabetes may suffer with wide range of complications that involves microvasculature related stroke, ischemic heart disease, diabetic retinopathy and nephropathy.[3] Others complications include periodontitis, neural disorders, gastroenteritis, delayed gastric emptying, renal disorders, dermatological manifestation, erectile dysfunction, diabetic retinopathy and diabetic macular edema.[4]

Medicinal herbs have played a significant role in treating and preventing a variety of diseases throughout the world. Conventional herbal therapy is tried globally to treat diabetes mellitus to delay the onset of diabetic complications and it also supply a great source of antioxidants which is helpful in preventing or delaying different diseases and their outcomes.[5] Their mechanism of action is based upon increasing insulin secretion, enhancing glucose uptake by adipose and skeletal muscle tissue, inhibiting intestinal glucose absorption and inhibiting hepatic glucose production.[6] One of the conventional herb used to treat diabetes mellitus is neem (Azadirachta indica). Azadirachta indica commonly

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known as neem has gained worldwide attraction in recent years, owing to its wide range of medicinal properties.[7] The world prefers the development of such drugs which have minimum toxic potential. [Azadirachta indica A. Juss] reportedly has various medicinal properties and has been in use in many continents for centuries. Pharmacological and biological effects are attributed to all parts and extracts of this plant, including antidiabetic, anti-inflammatory, antioxidant, antiplasmodial, antitrypanosomal, anticancerous, antimicrobial, spermicidal, anthelminthic, antifertility, immunomodulating, nematicidal, immunocontraceptive, insecticidal, and insect repellant effects.[8,9] Diabetic nephropathy is a very common complication of diabetes mellitus which is associated with high mortality and morbidity.[10] This study was aimed to determine and compare the nephroprotective effect of ethanolic extracts of leaves and seeds of azadirachta indica on serum urea and creatinine in diabetic albino rats. The assessment of the effects of this potential herbal medicine will allow clinicians to redesign preventive and therapeutic regime of a fairly common health disorder.

Material and Methods

The study was a randomized controlled trail carried out in Physiology department of services institute of medical sciences, Lahore from November 2018 to April 2019.

Adult and healthy male albino rats (One hundred and twenty) were housed in four groups of 30 per cage for minimally seven days prior the commencement of experiment. Dwelling environment was kept at 26±2 0C with 12-hour light/dark cycle.[11] The rats were categorized in four groups (each group containing 30 rats). Group 1: Normal control provided with normal saline orally

Group 2: Diabetic control was given normal diet. Group 3 (Experimental 1): got treatment with extract of Azadirachta indica leaves orally (500 mg/kg) daily for 28 days. Group 4 (Experimental 2): got treatment with extract of Azadirachta indica seeds orally (500 mg/ kg) daily for 28 days.

Results

In this randomized controlled trial, the effects of neem leave and seeds on the serum urea and creatinine profile of a total of 120 male diabetic albino rats were evaluated.

The serum urea and creatinine in diabetic control group was found to be highly significantly (p=0.000) greater than in the control group (Table 1). After administering neem leaves and seeds extract, the mean difference showed a highly significant (p=0.000) drop in urea and creatinine quantity in treated group compared to the untreated diabetic control group. (Table 2, 3).

The experimental group treated with neem leaves extract had non-significantly lower (p=0.000) serum urea levels than in the experimental group treated with neem seeds. However, difference of decreased serum creatinine between the two groups was non-significant (Table 4). Figure 1 shows mean urea and creatinine values in normal control, diabetic, and treatment groups.

Discussion

Alloxan monohydrate achieves its diabetogenic results by specifically destroying the pancreatic beta cells, but other endocrine cells and exocrine parenchymal cells were unaffected. The cytotoxic agent exerts its diabetogenic effects by reactive oxygen species which promptly destroys beta cells.[12] To induce diabetes, a single dose of alloxan monohydrate was given to overnight fasting rats of diabetic control and experimental groups before commencement of experiment.[12] At this dose (120 mg/kg), there is incomplete destruction of pancreatic beta cells which results in type 2 diabetes mellitus (NIDDM).[13] As Alloxan can lead to fatal hypoglycemia because of tremendous release of pancreatic insulin, rats were infused with 15-20 ml of 20% glucose solution intra peritoneally after 6 hours. To prevent hypoglycemia for next 24 hours the rats were kept on 5% glucose solution bottles.[14] Blood glucose was evaluated after 72 hours to confirm hyperglycemia.[15] Rats with hyperglycemia (>200 mg/dL) were considered diabetic and incorporated in experiment[16]. Then diabetic rats of group 3 and 4 were treated with leaves and seeds (ethanolic extract) of Azadirachta indica for 28 days.[17] On 29th day, intracardiac blood sample (4-5ml) was obtained to evaluate the effects of plant extract on renal profile.

Freshly matured leaves and seeds (5kg each) of Azadirachta indica were fetched locally from Lahore. Botanical identification of the leaves and seeds was completed in the Botany Department, Punjab University. An 80% ethanol extract of the air-dried and coarsely ground Azadirachta indica leaves and seeds was obtained via standardized Soxhlet extractor in Applied Chemistry Research Centre, PCSIR Labs, Lahore. The extract thus acquired, was subjected to filtration and ethanol (solvent)

evaporation in a rotary evaporator in a vacuum. A blackish-brown concentrate, obtained post-evaporation, was then preserved at 40^{0}C. Preceding to every dose, the crude extract was liquefying in sterilized distilled water and diluted to the required concentration.[18]

Initial blood sample was drawn aseptically from tail vein 72-hours after alloxan injection to confirm hyperglycemia. Sampling was repeated on the 29th day of the experiment after ensuring the animals were fasting overnight. Each rat was anesthetized using ether before drawing 5-milliliter blood from their tail vein. Four ml of each sample was allowed to coagulate at room temperature in the test tube for 30 minutes followed by centrifugation at 5000 rpm for 20 minutes. Post-centrifugation, the serum was collected and preserved in labeled tubes. It was kept at -20°C to be test urea and creatinine later on.[19] PASW[18] (formerly SPSS) was used to conduct data analysis. ANOVA test was carried out for descriptive analysis to find the arithmetic mean±SD values of obtained data. Post hoc Tukey's HSD test (multiple comparisons) was applied to find any significant value (p-value less than 0.05) among the four groups existed. The values were appraised highly significant when the p-value was less than 0.001.

The current study is focused to evaluate and compare the urea and creatinine lowering outcomes of ethanolic neem leaves and seeds extracts in alloxan induced diabetic rats. When induced with Alloxan, diabetic rats showed a rise in serum urea and creatinine levels (p= 0.001) compared to normal controls. The serum urea and creatinine reduced; in the experimental groups treated with the ethanolic extracts of neem leaves & seeds versus the untreated diabetic controls. Furthermore, the leaves extract was shown to have non significantly serum urea lowering effect than the seed extracts (p=0.000), but difference in decline of serum creatinine between two groups was non-significant. Similar results were obtained by Dholi et al[18], when alloxan induced diabetic rats were administered ethanolic extract of neem leaves for single dose therapy and multiple dose therapy for two weeks both leading to decline of urea and creatinine levels. Patel et al[19], administered neem extracts among few other herbal extracts for 42 days to diabetic rats that resulted in notable decline in the serum urea and creatinine levels. Kpela T[20], investigated the protective effects of neem on cisplatin-induced kidney damage and results showed that urea and creatinine levels were normalized by pretreatment with neem leaf extract. Hence, the results of our study indicate the potential serum urea and creatinine lowering benefits of using the Azadirachta indica in herbal medicine and warrants further research and human trials.

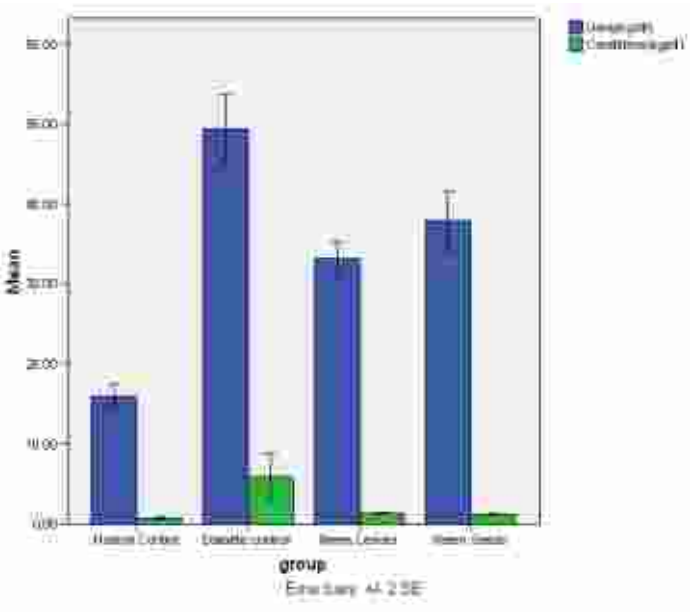

Figure 1: *Mean ± SEM serum urea and creatinine.*

Table 1: *Renal parameters in normal and diabetic control*

Renal profile	Group 1	Group 2	Mean difference	p-value
Urea(mg/dL)	16.00±4.00	49.33±11.61	33.33	0.000*
Creatinine (mg/dL)	0.71±0.28	5.95±7.86	5.24	0.000*

*Values are given as Mean ± SD: *p <0.001 highly significant*

Table 2: *Renal parameters in experimental group treated with neem leaves*

Renal profile	Group 2	Group 3	Mean difference	p-value
Urea(mg/dL)	49.33±11.61	33.20±5.62	16.13	0.000*
Creatinine (mg/dL)	5.95±7.86	1.34±0.28	4.61	0.000*

Values are given as Mean ± SD: *p <0.001 highly significant

Table 3: *Renal parameters levels in experimental group treated with neem seeds*

Renal profile	Group 2	Group 4	Mean difference	p-value
Urea(mg/dL)	49.33±11.61	37.90±10.15	11.43	0.000*
Creatinine (mg/dL)	5.95±7.86	1.21±0.30	4.74	0.000*

*Values are given as Mean ± SD: *p <0.001 highly significant*

Table 4: *Comparison of renal parameters between experimental groups (G3 and G4) treated with neem leaves seeds respectively*

Renal profile	Group 3	Group 4	Mean difference	p-value
Urea (mg/dL)	33.20 ± 5.62	37.90±10.15	4.70	0.142
Creatinine (mg/dL)	1.34 ± 0.28	1.21 ± 0.30	0.13	0.999

*Values are given as Mean ± SD: *p <0.001 highly significant*

Conclusion

The current research decides;

1. Ethanol based extracts of neem seeds and leaves are urea and creatinine lowering agents.
2. Leaves and seeds extract of Neem exhibited nephroprotective effect but do not show any significant difference in urea and creatinine lowering.

Conflict of Interest None

References

1. Guariguata L, Whiting DR, Hambleton I, Beagley J, Linnenkamp U, Shaw JE. Global estimates of diabetes prevalence for 2013 and projections for 2035. Diabetes research and clinical practice. 2014 Feb 1; 103(2): 137-49.
2. Artha IM, Bhargah A, Dharmawan NK, Pande UW, Triyana KA, Mahariski PA, Yuwono J, Bhargah V, Prabawa IP, Manuaba IB, Rina IK. High level of individual lipid profile and lipid ratio as a predictive marker of poor glycemic control in type-2 diabetes mellitus. Vascular Health and Risk Management. 2019; 15: 149.
3. Ngala RA, Awe MA, Nsiah P. The effects of plasma chromium on lipid profile, glucose metabolism and cardiovascular risk in type 2 diabetes mellitus. A case-control study. PloS one. 2018 Jul 5; 13(7):e0197977.
4. Mahboobi S, Rahimi F, Jafarnejad S. Effects of prebiotic and synbiotic supplementation on glycaemia and lipid profile in type 2 diabetes: a meta-analysis of randomized controlled trials. Advanced pharmaceutical bulletin. 2018 Nov; 8(4):565.
5. Shabani E, Sayemiri K, Mohammadpour M. The effect of garlic on lipid profile and glucose parameters in diabetic patients: A systematic review and meta-analysis. Primary care diabetes. 2019 Feb 1; 13(1):28-42.
6. Wajdy J. M, Tayseer A.T, Dheyaa K.O.Constituents, pharmacological and toxicological effects of Meliaazadirachta- A review. SMJ Vol 55 Issue 01 Jan 2021;
7. Vasanatha G, Venkatesham A, Dayakar C.H. Antihyperlipidemic Activity of ethanolic extract of MacrotylomaUniflorum (Lam.) Verdc. Leaves and Stems on High-Fat diet-induced hyperlipidemia. Int J of Green Pharmacy 2020; 14(1)93-97
8. Omonije OO, Saidu AN, Muhammad HL. Antidiabetic activities of chromolaenaodorata methanol root extract and its attenuation effect on diabetic induced hepato-renalimpairement in rats. ClinPhytosci 2019; 5-23.
9. Shabani E, Sayemiri K, Mohammadpour M. The effect of garlic on lipid profile and glucose parameters in diabetic patients: A systematic review and meta-analysis. Primary care diabetes. 2019 Feb 1; 13(1):28-42.
10. Kim KS, Lee JN, Park JH, Lee EY, Moon JS, Lee SK. Identification of novel biomarkers for early detection of diabetic nephropathy. Biomedicine 2021; 9(5), 457.
11. Pingali U, Ali MA, Gundagani S, Nutalapati C. Evaluation of the Effect of an Aqueous Extract of Azadirachta indica (Neem) Leaves and Twigs on Glycemic Control, Endothelial Dysfunction and Systemic Inflammation in Subjects with Type 2 Diabetes Mellitus–A Randomized, Double-Blind, Placebo-Controlled Clinical Study. Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy. 2020; 13:4401.
12. Airaodion AI, Olatoyinbo PO, Ogbuagu U, Ogbuagu EO, Akinmolayan JD, Adekale OA, Awosanya OO, Agunbiade AP, Oloruntoba AP, Obajimi OO, Adeniji AR. Comparative assessment of phytochemical content and antioxidant potential of Azadirachta indica and Parquetinanigrescens leaves. Asian Plant Research Journal. 2019 Mar 19:1-4.
13. Sadat AF, Sultana A, Rahman MA, Sharma D, Khan MA, Khan MM, Azad MA. Study of Hypoglycemic Properties of Aqueous Fresh Leaves Extracts of Azadirachta indica, Bryophyllumpinnatum, Carica papaya & Mikaniacordata Prepared by Ultrasound Assisted Extraction Method. International Journal of Innovative Science & Research Technology. 2021; 6(10):942-6.
14. Ezeigwe OC, Ezeonu FC, Okani CO, Onwusulu DN, Onuegbu ME. Aqueous extract of Azadirachta indica leaves favorably alters the course of streptozotocin-induced diabetes in rats: A comparative prospective cohort study. Biomedical Research and Therapy. 2020 Jul 31; 7(7):3877-89.
15. Saleem T, Mumtaz U, Bashir MU, Qureshi HJ, Saleem A. Comparison of hypoglycemic effects of Azadirachta indica seeds and leaves on alloxan induced diabetes in male albino rats. Pak J Med Health Sci. 2018 Apr 1; 12:753-6.
16. Ansari P, Hannon-Fletcher MP, Flatt PR, Abdel-Wahab YH. Effects of 22 traditional anti-diabetic medicinal plants on DPP-IV enzyme activity and glucose homeostasis in high-fat fed obese diabetic rats. Bioscience Reports. 2021 Jan; 41(1):BSR20203824.

17. Shahwan MJ, Jairoun AA, Farajallah A, Shanabli S. Prevalence of dyslipidemia and factors affecting lipid profile in patients with type 2 diabetes. Diabetes & Metabolic Syndrome: Clinical Research & Reviews. 2019 Jul 1; 13(4):2387-92.
18. Dholi SK, Raparla R, Mankala SK, Nagappan K. In vivo antidiabetic evaluation of neem leaf extract in alloxan induced rats. J App Pharm sci 2011; 01: 100-5.
19. Patel SS, Shah RS, Goyal RK. Antihyperglycemic, antihyperlipidemic and anti-oxidant effects of Dihar, a poly herbal ayurvedic formulation in stretozotocin induced diabetic rats. Indian J ExpBiol 2009; 47: 564-70
20. Kpela T, Ekanem TB, Akpantah AO. Protective effect of ethanol extract of neem leaves on cisplatin-induced kidney damage in wistar rats. Glob Adv Res J Med medical sci 2012; 1: 249-54.

Authors Contribution

TS: Conceptualization of Project
TS: Data Collection
AS : Literature Search
NS, NJ: Statistical Analysis
TS, AS: Drafting, Revision
NK, OI: Writing of Manuscript

Morbidity Pattern Among Hospitalized Children (1month To 5 Years) In A Tertiary Care Hospital

Shazia Naz,[1] Abeer Qadir,[2] Mohammad Abbas,[3] Roshnak Azam Khan,[4] Mohammed Ali Khan[5]

Abstract

Objective: To study the morbidity pattern among admitted children (1 month to 5 years) in a tertiary care hospital in order to find out the common illnesses and their relationship with the change in weather over a year.

Method: A retrospective observational study done in Pediatric unit, Punjab Rangers Teaching Hospital (PRTH), Lahore, over one year (1st Jan 2019-31st Dec 2019). All admitted children 1month - 5years of age were included. Newborns and children >5 years of age were excluded from study.

Data was collected from Medical Records of the admitted patients. Permission was taken from hospital ethical committee

Results: Total admissions in one year were 846, out of which 462 (54.7%) were children 1 month to 5 years of age. 267 children (57.7%) were males and 195 (42.2%) were females. Admissions due to acute respiratory tract infections (ARI) were 111 (24.0 %) and acute gastroenteritis (AGE) led to 138 admissions (29.8%). Together these two illnesses are responsible for almost half of the total admissions in this age group (53.8%). Admissions due to infectious causes were 83.3 % compared to 16.6% admissions due to noninfectious causes. It was observed that AGE was more prevalent in summer months ((May-August) and ARI being the leading cause in winter months (Nov-Feb). However, the association between AGE and ARI was not found to be significant.

Key Words: Morbidity pattern, Tertiary care hospital, Acute respiratory infection (ARI), Acute gastroenteritis (AGE)

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Introduction

Pediatric age groups (0 to 14 years) constitute nearly 43% of Pakistan's population, of which 15% are up to 5 years of age (34.88%).[1] This age group is vulnerable to multiple health related issues. Status of a child's health determines overall economic development and priorities of a community. It reflects a child's access to basic health and education facilities.

ARI and AGE are responsible for 76.5% of morbidity among pediatric age groups of up to 5 years at least once in 3 months.[2] Various health care programs are based on prevention and treatment of these two conditions. 3.5% of global burden of disease is caused by ARI. On an average, in developing countries each child has at least five episodes of ARI in a year.3 These preventable illnesses are responsible for 30 to 50% of total OPD visits and 20 to 30% of hospital admissions. Recent community based estimates from prospective study report 70% of childhood morbidities among children less than 5 years are due to ARI.[4] ARI and diarrheal diseases show seasonal variations.[5] Admissions due

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to ARI are maximum in the winter months and those due to AGE are more in the summer months. Both can be prevented and treated by simple, least expensive measures. Preventable infections are the major causes of morbidity and mortality in Children Emergency Room and children less than 5 years of age are commonly affected.[6] Awareness of seasonal variations can help physicians in counselling of patients and parents regarding preventive measures.[7] A hospital can be better equipped beforehand and optimal control measures can be taken well in time. Morbidity patterns among children can be determined following the indoor admissions in a tertiary care hospital. A tertiary care hospital provides basic and specialized healthcare facilities. Review of such information is helpful not only in accessing the healthcare system but at the same time it identifies the loopholes in the existing system, thus helpful in formulating guidelines for future planning. Overall economic burden due to illnesses which can be easily prevented and treated is massive. Simple preventive measures like health education regarding personal hygiene, provision of clean drinking water and improving sanitary conditions can be helpful. Promotion of breast feeding and vigilant immunization programs can also prevent such illnesses. Morbidity pattern is not static and is dependent on provision of basic healthcare facilities, ensuring the preventive measures and certain environmental factors as well. Medical records can help in determining the disease burden and health care needs of the community and the adequacy of health care resources.[8] Proper documentations is therefore important for better health care planning and appropriate resource allocation for improving health care facilities.

Pakistan being an underdeveloped country lags behind in provision of basic healthcare to the pediatric age group despite all its efforts. Identification of the disease trends can be helpful in determining the effects of already existing health programs. Future planning and implementation efforts are also based on such studies.

Material and Methods

This retrospective observational study was conducted at PRTH. It provides all basic and specialized healthcare facilities to Rangers employees, their families and general public. Department of Pediatrics at PRTH-has a general Pediatrics ward besides a well-established neonatal unit. General Pediatrics ward has a well-equipped High dependency Unit (HDU). Patients are admitted through OPD as well as through emergency. This data was collected in the initial year of the hospital's inauguration as a tertiary care facility. All cases of pediatric inpatients (1 month to 05 years of age) between 1st January 2019 and 31st December 2019 have been included in the study. Neonates and Pediatric patients older than 5 years of age were excluded from the study. Data was collected from medical records of admitted patients. Morbidity pattern among these admitted cases was studied according to parameters of age, gender, infectious versus noninfectious causes and seasonal variations in the most common causes of admissions.

Results

Total admissions in one year (1st Jan-31st Dec 2019) were 846, out of which 462 were children >1 month to 5 years of age (54.7%). 267(57.7%) were male and 195 (42.2%) were female patients. Male children outnumbered female cases throughout the year except in the month of February. Total admissions due to infectious causes were 83.3 %, with only 16.6 % admissions were due to noninfectious causes. ARI and Diarrhea constitute 53.8% of total admissions in a year. It was observed that AGE being more prevalent (41.7%) in summer months (May-August) and ARI being the leading cause (43.5%) in winter months (Nov-Feb). (Fig-1) The mean admissions with ARI are 9.2 and median 9.0, ranging from 1-21 with standard deviation of 6.0. 5 admissions were in 25th centile, 9 in 50th centile and 11.7 in 75th centile. Mean admissions with AGE are 11.0 and median

Table 1: *Month-wise Distribution of cases according to age*

Month	(1 mo - 5 yr)	>5 yrs	Total admissions	% of <5yrs
Jan	38	42	80	47.5
Feb	23	18	41	56
Mar	34	33	67	50.7
April	47	31	79	60.7
May	70	24	96	75
June	33	21	54	61
July	42	38	80	52.5
August	42	31	75	58.6
September	32	25	57	56.1
October	22	50	72	30.5
November	37	36	74	51.3
December	42	35	77	54.5
Total	**462**	**384**	**852**	**54.9**

is 9.0 ranging from with a standard deviation of 8.89. The Pearson correlation of ARI versus AGE is negative at -0.261, and 2-tier value is 0.412 which is not significant. This is again seen when Chi Square test was applied, 0.355 in ARI and 0.343 in AGE. (Fig-2). Besides ARI and AGE, children in this age group were also admitted with other infectious diseases like Enteric fever, Acute Viral Hepatitis, Meningitis and Urinary Tract Infection. (Fig-3) Among noninfectious causes of admission, malnutrition and iron deficiency anemia were common. Children with chronic illnesses like congenital heart disease, nephrotic syndrome, chronic kidney disease, epilepsy and cerebral palsy were also admitted. Noninfectious illnesses contribute to only 16.6% of total admissions.

Out of the total admissions, 54.9% were of the children 1 month to 5years.

Table 2: *Distribution of cases according to gender (n= 462)*

Month	Male	Female
Jan	24	14
Feb	10	13
Mar	20	14
April	26	22
May	53	19
June	14	19
July	24	18
August	25	19
September	17	15
October	12	10
November	20	18
December	24	18
TOTAL	**269**	**199**

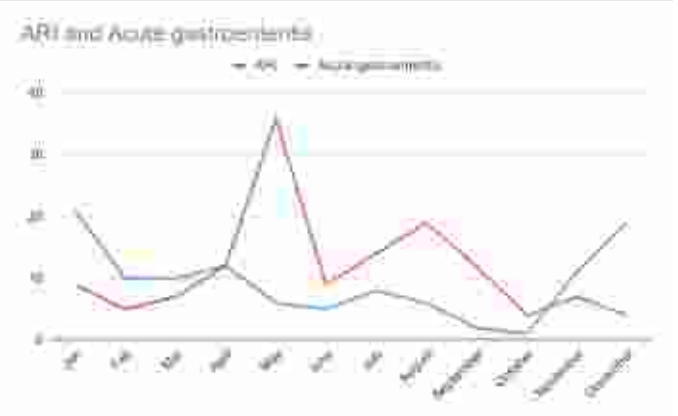

Fig-1: *Admissions due to Acute respiratory infection and Acute gastroenteritis*

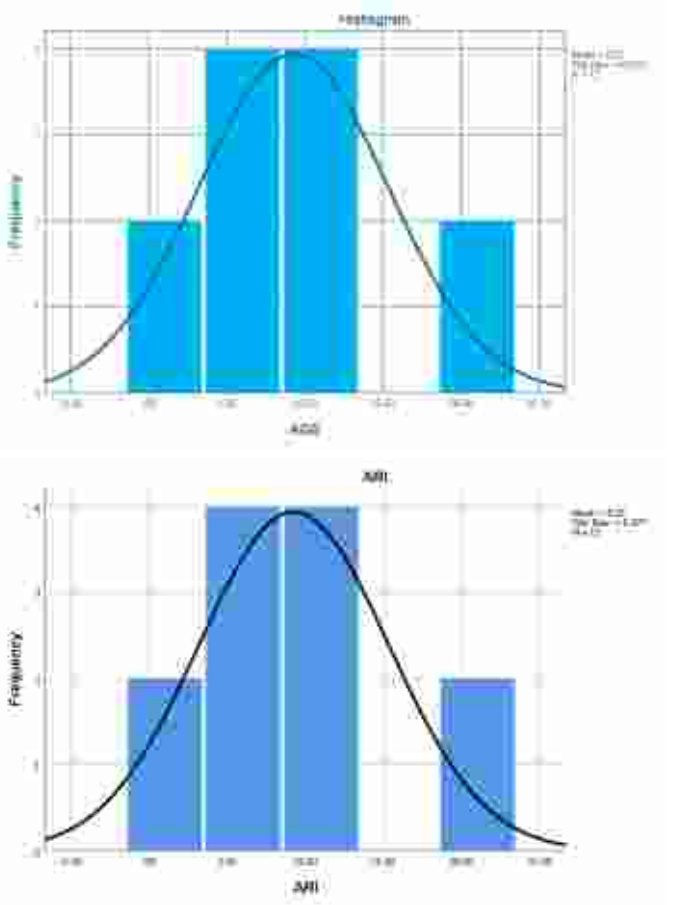

Fig-2: *Frequency of AGE and ARI over 12 months*

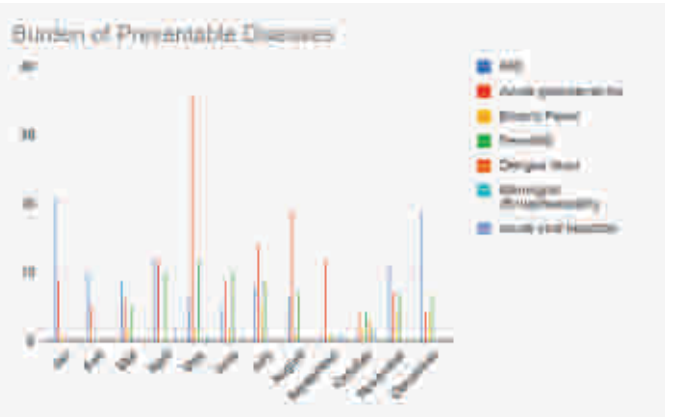

Fig-3: *Burden of preventable disease*

Discussion

Status of child health care in Pakistan is grave. In our study 24.0% and 29.8 % children were admitted with ARI and AGE respectively in a year, which signifies the fact that diarrhea and ARI are the leading causes of childhood morbidity in children till 5 years of age. Morbidity in all age groups was maximum due to Acute Respiratory Infections (ARI), with overall morbidity

of 43.4% followed by Acute Diarrheal Diseases (16.8%) in a similar study done at Uttar Pradesh, India.[8] In our study these two illnesses constitute 53.8 % of total admissions in a year. In our study 41.4% of admissions of ARI were due to upper respiratory tract infections and the rest (58.5%) were lower respiratory tract infections.

Most of the admissions with gastroenteritis were acute cases (98.6%. Due to the study being conducted in the inaugural year of hospital as a tertiary care facility, chronic cases of gastroenteritis (1.4%) were still new to follow-up and work-up was in progress. A number of these patients were readmitted more than once with similar complaints in this one-year study. It was observed that AGE is more prevalent in summer months ((May-August) and ARI being the leading cause in winter months (November -February). A study by Gowa et al reveals that respiratory tract infections was most common (41.2%) in the last quarter of the year (Oct - Dec) and AGE during the second quarter (38.7%). Together these 2 illnesses form the majority of Emergency department burden.[9] In a study conducted in Multan, Pakistan by Tayyaba Amin and Shahid Iqbal it was found out that bronchiolitis started in October and November. Maximum number of cases due to ARI were observed in December, January and February, with minimal cases in June, July and August.10 Majority of patients admitted in summer months were of AGE with peak during July-August. Respiratory illnesses mostly presented in January and March.[11] Similar observations was made in our study also. This is multifactorial due to extremes of weather, lack of sanitation, improper health education and facilities. A better understanding of seasonal infectious disease outbreaks and persistence is likely to result in better understanding of the optimal control strategies.[12] A hospital can be better equipped and prepared beforehand to control and manage such outbreaks. As both the illnesses can be prevented by simple measures, the need of appropriate health education is highly recommended.

Other common causes of childhood illnesses are also communicable and preventable. At Least 7 out of 10(70%) most common diseases were of infectious origin.[13] It was found in our study that 83.3 % of total admissions were due to an infectious disease. Fever is one of the most common presenting complaints in childhood and most frequently is due to an infection.[14] Preventable infections are the major causes of morbidity and mortality among children less than 5 years of age.[6]

Simple preventive measures like health education regarding personal hygiene, provision of clean drinking water and improving sanitary conditions can be helpful. Promotion of breast feeding and vigilant immunization programs can also prevent such illnesses. Good health, good immunity and clean environment is required in preventing pneumonia[9] Likewise, Diarrhea is both preventable and treatable by simple and less costly measures. In USA, gastroenteritis accounts for 10% of hospital admissions. Most children affected with diarrhea are not dehydrated and can be managed at home. Worldwide most cases are due to viral infections.[15] Sanitation and hygiene are particularly important in institutions, including schools and hospitals where nosocomial infections are common. Repeated GI infections lead to impaired immunity and malnutrition. Diarrhea and fever can result in long term health effect, including depletion of immune strength, malnutrition and making children susceptible to other diseases.[16] In our study it was observed that patients admitted with ARI and AGE also had clinical signs of anemia and malnutrition. Similarly, children with chronic illnesses also had signs of nutritional deficiencies and presented with failure to thrive. Thus, childhood illnesses can have both short- and long-term implications. Overall impact will be less productivity and economic burden. Simple protective, preventive and treatment solutions do exit. All can be achieved by breast feeding, proper nutrition and promoting hand washing.[3] Some factors found to significantly influence the healthcare-seeking pattern were age and sex of the children, nutritional score, age and education of the mother, wealth status and access to electronic media.[17] ARI in this age group is caused by bacterial pathogens like H. Influenza and S. pneumonia. Both can be prevented by effective immunization. Likewise, ARI due to pertussis, measles and diphtheria can also be reduced.[18] In our study 41.4% of admissions of ARI were due to upper respiratory tract infections and the rest (58.5%) were lower respiratory tract infections, however due to limitation of resources, as in all developing countries, the exact pathogen was not identifiable.

Understanding the seasonal variations among these two common illnesses will also help in designing protocols for the proper management of the common ailments, health education and advocacy as it may apply.[6] In our study, beside ARI and AGE, children in this age group were also admitted with other infections like Enteric fever, acute viral Hepatitis, nonspecific fever and CNS infections, fever being the presenting symptom in most of these diseases.

Admissions due to infectious and communicable disea-

ses were 5 times more than noninfectious diseases (83.3%) as shown in this study. Amongst the other causes of morbidity in the pediatric age group, anemia was most prevalent, with overall 6.5% of children admitted due to severe anemia.[8] In our study, iron deficiency anemia (IDA) was prevalent in 1.94% of total admitted patients. The prevalence of IDA amongst Pakistani children represents a moderate burden that disproportionately affects the youngest, growth retarded children, affected children are more likely to have mothers with IDA and live in areas where food security is lacking.[19] Malnutrition and iron deficiency anemia collectively constitute 3.45 % of all admissions. Clinical signs of anemia and malnutrition were also noticed in children admitted with repeated ARI and AGE and among children with chronic illnesses. In a study conducted at Lahore by Zaman et al, vaccine-preventable diseases were only 0.5% of the total. Anemia and rickets were rare (2.0%), but commonly seen among the nutritional deficiencies.[(20)] Other important causes of morbidity in under-5 age group were cardiovascular system (CVS) diseases constituting 5.9%, followed by neurologic diseases (3.7% admissions).[8] In our study, CVS diseases were responsible for 1.29% cases, hematological other than IDA and kidney diseases were responsible for 2.59 % and 1.29%% of total admissions, respectively. CNS disorders other than infections form 4.11% of total admissions.

Of the total admissions in a year, 54.6 % of patients were less than 5 years of age, with more than half of these (58.8%) were in the age group 1 month to 2 years. Majority of the admissions in this age group was with acute gastroenteritis and ARI. Children less than five years were responsible for 80.1% of all admissions, while those less than two years accounted for 56.8%, as shown in a study done in Nigeria.[21] Similar observations was made by Srivastav et al as admissions in under-5 age group were maximum below 12 months of age (26.8%) followed by 20.9% admissions in 3–4-year age group.[8]

Hospital records can help in accessing the morbidity pattern which will determine the health care needs of the community and check the effectiveness of already planned health care facilities.[(8)] Understanding the epidemiological trends in hospital admission is vital for health care planning, resource allocation and improving existing service facilities. Disease spread can be traced, notified and spread can be controlled in this way. Such studies can form the basis for developing nationwide recommendations for improving healthcare in children.

The common causes of morbidity among children in this age group as observed in our study can be avoided by implementing primary health care programs. Intensification of the actions recommended by the programs directed to child health is all that is required.[22]

Conclusion

Hospital records can help in determining the common causes of morbidity. In this study it is observed that ARI and Diarrhea are still the leading causes of childhood morbidity and hospital admissions. Both are infectious, affected by change in weather but can be easily prevented by taking simple measures. Huge burden on the already limited economic resources can be lessened by proper planning and implementation of already existing preventive strategies. Such studies can provide the foundation for crafting recommendations for improving health care in children.

References

1. Pakistan Bureau of Statistics, Government of Pakistan. Population by 5-year age group. Census 2017 report.
2. Shinde M, Joshi A, Trivedi A. Morbidity profile of preschool children in rural area of central Madhya Pradesh. Int J Community Med Public Health. 2015 Aug;2(3):298-301. http://dx.doi.org/10.18203/2394-6040.ijcmph20150486
3. Rudan I, Boschi-Pinto C, Biloglav Z, Mulholland K, Campbell H. Epidemiology and etiology of childhood pneumonia. Bull World Health Organ. 2008 May; 86(5): 408-16. doi: 10.2471/blt.07.048769. PMID: 18545744; PMCID: PMC2647437.
4. Dongre AR, Deshmukh PR, Garg BS. Health expenditure and care seeking on acute child morbidities in peri-urban Wardha: a prospective study. Ind J Pediatr. 2010 May;77(5):503-7. doi: 10.1007/s12098-010-0063-8. Epub 2010 Apr 17. PMID: 20401704.
5. Schrijver TV, Brand PL, Bekhof J. Seasonal variation of diseases in children: a 6-year prospective cohort study in a general hospital. Eur J Pediatr. 2016 Apr; 175(4):457-64. doi: 10.1007/s00431-015-2653-y. Epub 2015 Oct 22. PMID: 26494134.
6. Ezeonwu B, Chima O, Oguonu T, Ikefuna A, Nwafor I. Morbidity and mortality pattern of childhood illnesses seen at the children emergency unit of federal medical center, asaba, Nigeria. Ann Med Health Sci Res. 2014 Sep; 4(Suppl 3):S239-44. doi: 10.4103/2141-9248. 141966. PMID: 25364596; PMCID: PMC4212384.

7. Seema N,Khan H, Jiskani AR, Saboohi E, Channa Y, Maqsood S, Tariq A, Khan T. Seasonal variations among admitted Pediatric patients at tertiary care hospital, Gadap Town,Karachi, Pakistan. Int J Res Med Sci. 2019 Aug;7(8):2945-2949. http:// dx.doi.org/ 10.18203/2320-6012.ijrms20193374
8. Srivastav S, Kariwal P. Morbidity pattern of hospitalised children in under 5 age group in a tertiary care hospital: A retrospective overview. Ind J. Mat Chi Health. 2018 Mar; 13(4):1-7
9. Gowa M, Habib I, Tahir A, Yaqoob U, Junejo S. Disease Spectrum and Frequency of Illness in Pediatric Emergency: A Retrospective Analysis From Karachi, Pakistan. Ochsner J. 2019 Winter;19(4):340-346. doi: 10.31486/toj.18.0134. PMID: 31903057; PMCID: PMC6928663.
10. Amin T, Iqbal S,Saleem I. Seasonality of bronchiolitis in hospitalised children, Multan, Pakistan. Eur Res J. 2015,46:PA1335. DOI: 10.1183/13993003. congress-2015.PA1335
11. Black RE, Cousens S, Johnson HL, Lawn JE, Rudan I, Bassani DG, Jha P, Campbell H, Walker CF, Cibulskis R, Eisele T, Liu L, Mathers C; Child Health Epidemiology Reference Group of WHO and UNICEF. Global, regional, and national causes of child mortality in 2008: a systematic analysis. Lancet. 2010 Jun 5; 375(9730): 1969-87. doi: 10.1016/S0140-6736(10)60549-1. Epub 2010 May 11. PMID: 20466419.
12. Grassly NC, Fraser C. Seasonal infectious disease epidemiology. Proc Biol Sci. 2006 Oct 7;273(1600): 2541-50. doi: 10.1098/rspb.2006.3604. PMID: 16959647; PMCID: PMC1634916.
13. Peltola H. Observations on the seasonal variation of the most common acute pediatric diseases in the Helsinki area (Finland). J Community Health. 1982 Spring; 7(3): 159-70. doi: 10.1007/BF01325512. PMID: 7076880.
14. Soon GS, Laxer RM. Approach to recurrent fever in childhood. Can Fam Physician. 2017 Oct; 63(10): 756-762. PMID: 29025800; PMCID: PMC5638471.
15. Elliott EJ. Acute gastroenteritis in children. BMJ. 2007 Jan 6;334(7583):35-40. doi: 10.1136/ bmj.39036.406169.80. PMID: 17204802; PMCID: PMC1764079.
16. Takele K, Zewotir T, Ndanguza D. Risk factors of morbidity among children under age five in Ethiopia. BMC Public Health. 2019 Jul 15;19(1):942. doi: 10.1186/s12889-019-7273-4. PMID: 31307433; PMCID: PMC6631490.
17. Chinawa JM, Aniwads EC, Ugwunna NC. Pattern and prevalence of common pediatric illnesses presenting in a private hospital Onitsha, Southeast Nigeria. Curr Pediatr Res 2018; 22(1): 88-94.
18. Adegbola RA, Mulholland EK, Secka O, Jaffar S, Greenwood BM. Vaccination with a Haemophilus influenzae type b conjugate vaccine reduces oropharyngeal carriage of H. influenzae type b among Gambian children. J Infect Dis. 1998 Jun;177(6):1758-61. doi: 10.1086/517440. PMID: 9607866.
19. Habib MA, Black K, Soofi SB, Hussain I, Bhatti Z, Bhutta ZA, Raynes-Greenow C. Prevalence and Predictors of Iron Deficiency Anemia in Children under Five Years of Age in Pakistan, A Secondary Analysis of National Nutrition Survey Data 2011-2012. PLoS One. 2016 May 12;11(5):e0155051. doi: 10.1371/ journal.pone.0155051. PMID: 27171139; PMCID: PMC 486 5153.
20. Zaman S, Jalil F, Karlberg J, Hanson LA. Early child health in Lahore, Pakistan: VI. Morbidity. Acta Paediatr Suppl. 1993 Aug;82 Suppl 390:63-78. doi: 10.1111/ j.1651-2227.1993.tb12907.x. PMID: 8219468.
21. Okechukwu AA, Nwalozie C. Morbidity and mortality pattern of admissions into the Emergency Paediatric Unit of University of Abuja Teaching Hospital, Gwagwalada. Niger J Med. 2011 Jan-Mar;20(1):109-13. PMID: 21970271.
22. Oliveira RR, Costa JR, Mathias TA. Hospitalization of children under five years of age due to avoidable causes. Rev Lat Am Enfermagem. 2012 Jan-Feb; 20(1):135-42. English, Portuguese, Spanish. doi: 10.1590/s0104-11692012000100018.PMID: 22481731.

Authors Contribution

SN: Conceptualization of Project
RAK: Data Collection
MA: Literature Search
AQ: Statistical Analysis
MAK: Drafting, Revision
SN: Writing of Manuscript

Single Shot Tract Dilatation During Percutaneous Nephrolithotomy: Our Experience

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Abstract

Objective: To compare safety and efficacy of one-shot dilation and Alken sequential dilatation in PCNL

Method: This prospective study conducted on 60 renal stones patients underwent supine PCNL at Department of urology, Lahore General Hospital, Lahore from June 2020 to July 2021.Tract dilatation was performed using Alken dilatation (Group A, 30 patients) or One-shot dilatation (Group B, 30 patients).

Results: The mean age of patients in Group A and Group B were comparable (P=0.78). Stone clearance between group A and B was not different (86.7% v 83.3% respectively, p=1). Group B had a lower mean fluoroscopy time than group A. (124.13±22.40 Sec Vs 102.16±32.26 Sec, P=.003). Mean tract dilatation was shorter in group B than group A (5.06 ±0.80 min Vs 5.94 ±0.87 min, p<.001). Mean hemoglobin drop was similar in both groups (1.62±.56 g/dl Vs 1.38 ±.36 g/dl, P=.055). The complications among the groups were not significantly different.

Conclusion: One-Shot dilatation is a safe and effective technique for creation of nephrostomy tract in PCNL. That can reduce tract dilatation time and X-rays exposure time.

Keywords: PCNL, Tract dilatation, One-shot dilatation.

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Introduction

Nephrolithiasis is common urological problem, with worldwide prevalence ranging from 2 to 20%.[1] The life time risk of developing renal stones is 12% for men and 5% for women.[1] Incidence of renal stones is high in Pakistan as it located in the geographic region called the "stone belt" extends from Egypt and Sudan into the Middle East, India, Pakistan, Myanmar, Thailand and Indonesia.[2] Percutaneous nephrolithotomy (PCNL) portrayed within the 1980s revolutionized the treatment of kidney stones and still remains a vital treatment tool.[3]

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This minimally invasive surgery has emerged to become the preferred approach for treatment of large size renal stones and has superseded the open surgery for nephrolithiasis. This approach has replaced open renal surgery for stones. In selected cases RIRS (retrograde intrarenal surgery) might be a viable alternative to PCNL.[4,5] PCNL involves entering the renal collecting system with an access needle and guide wire, followed by tract dilation.[3] After appropriate tract dilation, a suitable size Amplatz sheath is introduced over dilators which make it easier to insert endoscope, working instruments, and nelaton catheter for stone wash out during procedure and placement of nephrostomy tube after completion of procedure.[6]

Recent studies agree that renal puncture and tract dilatation is a critical and fundamental step in PCNL and may be fulfilled by utilizing Amplatz dilators (semi rigid polyurethane facial dilators), Alken dilators (metal telescopic coaxial dilators), balloon dilator, or one-shot dilator.[7]

Alken dilators are more economical because of their

re-usability, and maintaining tamponade impact during dilatation of the tract.[8] Amplatz dilators are not reusable and may cause more blood loss due to consecutive dilator exchange which causes displacement of tamponade effect on paranchymal tract. The use of Alken and consecutive Amplatz dilators takes more time and are time-consuming, with a higher frequency of guide wire kinking during tract development.[8]

Minimizing X-rays exposure and blood loss are of prime importance during PCNL, and therefore balloon dilation is nowadays being considered as one of the methods for tract dilatation as it helps in reducing the X-rays exposure time during tract dilatation. Similarly, because of the steady pressure applied at the time of tract dilatation to the parenchyma of kidney, the rate of blood loss is decreased due to the tamponade effect. The drawbacks of this method are its cost as it is disposable.[9] In 2001, Frattini et al. conducted a study in Italy; they state that; one-shot dilation is easy to performed in majority of the patients. This method is as safe and effective as the balloon dilatation which is the gold standard but this method of dilatation can be performed in short time and with low cost than balloon dilatation.[10] In routine, Alken dilators are used for tract dilatation in PCNL but they are time consuming. The objective of this research was to compare outcomes of one-shot renal dilation and Alken dilatation in terms of tract dilation fluoroscopy time, hemoglobin decrease, hematoma formation, visceral injuries, urinoma formation, stone clearance and conversion to open surgery.

Material and Methods

This prospective study was conducted on 60 renal stones patients underwent PCNL at urology department, Lahore General Hospital, Lahore from June 2020 to July 2021. A thorough history was obtained, and a physical examination was carried out. Routine tests for anesthetic fitness were done and some specific investigations was performed i.e. urine culture & sensitivity, USG KUB, plain X-rays KUB, IVU and CT KUB was done if needed. Selected patients were randomly assigned into two equal groups, group A and B (30 patients in each group) by using computer generated table. In Group "A", Alken dilators were used, while in Group "B", one-shot procedure was employed. All procedures underwent under general endotracheal anesthesia in Galdakao- modified supine Valdivia position. Each procedure was carried out by the same surgical team. An open-ended **6**Fr ureteric catheter was placed into the collecting system retrogradly by using cystoscope. After injecting of the contrast dye through ureteric catheter under fluoroscopic guidance puncture of an appropriate calyx to the renal collecting system done with an 18 gauge Chiba needle. In some difficult cases access to the renal collecting system was achieved with combined ultrasound and fluoroscopic guidance.

Following the puncture of the renal collecting system, a 0.035-inch guide wire was passed through needle to collecting system. Then an 8 Fr olive tip was advanced over guide wire. In group A dilatation was carried out with six to seven consecutive dilators under fluoroscopy guidance. Eventually the tract dilated between 27Fr and 30Fr. In group "B" tract dilatation was performed under fluoroscopy guidance by directly advancing of a single 28Fr Amplatz dilator over 8Fr Olive tip dilator. During procedure tract dilatation fluoroscopy time was recorded from the time of guide wire insertion until placement of the sheath. Hemoglobin of the patients was checked pre operatively, Post-operative (immediately), and after 24 hours of surgery. Patients were evaluated for stone clearance during operation by fluoroscope and at first operative day by KUB X-rays or ultrasound. Patients were evaluated for any collection (hematoma, urinoma) at first operative day. For diagnosis of pleural injuries intra operative fluoroscopy was done, if the patient became symptomatic post-operatively, chest x-ray was performed. Patients were evaluated clinically for abdominal visceral injuries post operatively. Any suspected abdominal visceral injury was evaluated with contrast enhanced CT abdomen.

Data were entered and analyzed by using SPSS 24.0 version. Quantitative variables such as age, hemoglobin decrease and tract dilation fluoroscopy time were described as Mean ± S.D. for each group. Qualitative variables like gender, presence of hematoma, urinoma formation, visceral injuries, stone clearance and conversion rate were described as percentage.

Mean of hemoglobin decrease in each group were compared with Independent t test. Mean of tract dilation fluoroscopy time among both groups were compared with Independent t test. Presence of hematoma, urinoma formation, visceral injuries, stone clearance and conversion to open surgery in each group were compared with Chi-square test. For both the independent t test and the Chi-square test, a P-value of less than 0.05 was considered significant.

Results

The mean age of patients in group A was 41.16 ± 11.48 while the mean age in group B was 41.96±11.18 years (P=0.78). There were 35 males (58.3%) and 25 females (41.7%) among the patients. In group A male to female ratio was 19/11, In group B it was 16/14 (P=0.43) Table 1.

In Group A the mean of nephrostomy tract dilatation time was 5.94 ± 0.87 min while in Group B mean tract dilatation time was 5.06 ± 0.80 min (P<.001). In Group A the mean fluoroscopy time was 124.13 ± 22.40 Sec and range was (70-200) Sec. In Group B mean was 102.16± 32.26 Sec and range was (50-190) Sec (P=.003). Drop of hemoglobin was compared in both groups, In Group A the mean drop of hemoglobin was 1.62 ± .56 g/dl and 1.38 ± .36 g/dl in Group B (P=.055).

Stone free rate in Group A was 86.7% and in Group B was 83.3%, P value was 1.000 which is statistically not significant. Hematoma formation, urinoma formation and visceral injuries were not reported in all study population. These complications were not occurred in both groups. Conversion to open surgery was reported in (3) cases (5%) in all study population, 2 cases (6.7%) in group A and 1 case (3.3%) was in Group B (p= 0.554). Table 2

Table 1: *Comparison of demographic Characteristics of patients in groups.*

	Group A (Alken Serial dilatation, n=30)	Group B (One-shot dilatation, n=30)	P Value
Mean age (year ± SD)	41.16 ± 11.48	41.96 ± 11.18	0.78
Male Gender	19(63.3%)	16(53.3%)	0.43
Female Gender	11(36.6%)	14(46.6%)	0.43

Table 2: *Comparison of demographic Characteristics of patients in groups.*

	Group A (Alken Serial dilatation, n=30)	Group B (One-shot dilatation, n=30)	P Value
Mean Nephrostomy tract dilatation time (min ± SD)	5.94 ± 0.87	5.06 ± 0.80	<0.001
Mean Tract dilatation fluoroscopy time **(Sec ± SD)**	124.13±22.40	102.16±32.26	0.003
Mean Drop of hemoglobin **(g/dl ± SD)**	1.62± 56	1.38 ± .36	0.055
Stone free rate	26(86.7%)	25(83.3%)	1.000
Conversion to open surgery	2(6.7%)	1(3.3%)	0.554

Discussion

Dilatation of the tract is very important step in PCNL as it may cause hemorrhage, so selection of an appropriate dilatation system is necessary.[10] Traditionally Amplatz dilator and Alken dilator systems are used for tract dilatation in PCNL.But their main problem is the incremental nature which results in extended tract dilatation time, increased radiation exposure and also increases the risk of tract displacement.[10] Using Balloon dilator for PCNL tract creation helps to prevent renal displacement and kinking of guide wire during dilatation of tract. But due to high cost, it cannot be used regularly and it also found to have 17% of failure rate which may goes up to 25% in patients with previous renal surgery.[11] During the last few years, working has been done to perform tract dilatation with technique such as single-step dilation of the tract to be simple in use, having low cost, suitable for all patients with decreasing of complications like hemorrhage and radiation exposure. Frattini and colleagues used the novel one-shot technique with 26Fr-30F Amplatz dilator for nephrostomy tract creation. They used this method in 26 patients, the parameters, like exposure of radiation, blood loss, and used costs were analyzed and compared with other to groups; Alken metal telescopic dilator group, and balloon dilator group. They stated that one-shot dilation is easy to use, more secure, less time-consuming, and cheaper technique. However, they found that their research lacked a sufficient number of patients and the technique was not tried in patients who had previous kidney surgery.[10]

Penbegul et al used novel PCNL set (Ecoset) in 42 patients; which comprises of a single 30-F dilator, 30-F sheath, and 8-F polyurethane dilator. They concluded that; Ecoset is safe and feasible technique to be used in almost every adult patient for the tract dilation in PCNL [(12)]. Recent studies have shown that OSD is safe and effective for access to the renal collecting system. In meta analyses on comparison of tract dilatation methods in PCNL by Peng et al and Chiancone et al reported that OSD can reduce access time, fluoroscopy time and drop in hemoglobin. But there was no difference in stone clearance, transfusion rate and complications rate.[13,14] The results of these studies are same as in our study regarding fluoroscopy time, access time stone free rate and complication rate but no significant

diffidence in hemoglobin drop between groups in our study. In a recent retrospective study by Sharma et al on 70 patients undergoing PCNL, they compared single step dilatation and serial dilatation and reported that of using single step dilator can decrease radiation exposure and operation time.[15]

Girisha et al. concluded that; One-step dilatation is a safe, cost effective and easily accomplished technique with additional benefits of little tract dilatation time, less X-rays exposure and less chance of blood transfusion.[16] Suelozgen et al concluded that single step dilatation is safe and effective alternative for nephrostomy tract dilatation in adults.[17] Srivastava and colleagues compared sequential facial dilation and one-shot dilation in 100 patients of pediatric age group. They said that OSD is feasible and safe method in children reducing X-rays exposure and operative time.[18] Ganesh and associates concluded that; In patients who had previous open surgery for kidney stone of the same side, the single-shot dilation procedure is just as successful, safe, and well tolerated as the Alken dilation method.[19]

In a study conducted by Mohyelden et al on 150 patients, concluded that OSD is efficient as MTD during PCNL while patients in Barts flank-free modified supine position, with less dilatation time, X-ray exposure, blood loss, and hospital stay than MTD.[20]

Arslan and colleagues used One-shot multi access PCNL; they concluded that it can be safely performed for complex kidney stones due to its high clearance rates, despite some potential complications.[21]

In our study, no difference was found between the groups concerning the bleeding and changes in hemoglobin level. But difference in tract creation time and X-rays exposure time were significant.

Conclusion

Our findings demonstrate that one-shot dilatation is a safe and efficacious method of tract dilation that lowers both tract dilatation and X-ray exposure time. No differences were observed in decreasing of hemoglobin levels post-operatively, the successful dilation rate, and stone-free rate between the two techniques of tract dilatation.

References

1. Walker V, Stansbridge EM, and Griffin DG. (2013). Demography and biochemistry of 2800 patients from arenal stones clinic. Annals of Clinical Biochemistry 50(Pt 2): 127–139.
2. Ahmad S, Ansari TM, Shad MS. Prevalence of renal calculi; type, age and gender specific in Southern Punjab, Pakistan. Professional Med J 2016;23(4):389-395.
3. D'Arcy FT, Lawrentschuk N, Manecksha RP, Webb DR., Renal tract creation for percutaneous nephrolithotomy: the history and relevance of single stage dilation. Can J Urol. 2015 Oct; 22(5):7978-83.
4. Stern KL, Sivalingam S. Retrograde intrarenal surgery versus percutaneous surgery: do we have a winner? Minerva Urol Nefrol 2018;70:4–5.
5. Barone B, Crocetto F, Vitale R, Di Domenico D, Caputo V, Romano F, et al. Retrograde intra renal surgery versus percutaneous nephrolithotomy for renal stones >2 cm. A systematic review and meta-analysis. Minerva Urol Nefrol 2020;72:441–50.
6. Smith AD, Preminger GM, Kavoussi LR, Badlani GH., & Rastinehad, A. R. (2019). Smith's textbook of endourology 4th edition. Hoboken: Wiley-Blackwell, PP 232, 241
7. Nalbant I, Karakoyunlu AN, Yesil S, Ekici M, Zengin K, Ozturk U, Imamog˘lu MA. (2016). Comparison of Dilation Methods in Percutaneous Nephrolithotomy: Which One Is More Successful? Journal of laparoendoscopic & advanced surgical techniques; 26; 6.
8. Nour HH, Kamal AM, Zayed AS, Refaat H, Badawy MH, El-Leithy TR. (2014). Single-step renal dilatation in percutaneous nephrolithotomy: A prospective randomised study. Arab J Urol; 12(3):219-22
9. Srivastava A, Singh S, Dhayal IR, Rai P. A prospective randomized study comparing the four tract dilation methods of percutaneous nephrolithotomy.word J Urol. 2017May:35(5):803-807
10. Frattini A, Barbieri A, Salsi P, Sebastio N, Ferretti S, Bergamaschi E, Cortellini P., One shot a novel method to dilate the nephrostomy access for percutaneous lithotripsy, J Endourol. 2001 Nov; 15(9):919-23.
11. Joel AB, Rubenstein JN, Hsieh MH, Chi T, Meng MV, Stoller ML. Failed percutaneous balloon dilation for renal access: incidence and risk factors. Urology. 2005; 66(1):29-32.
12. Penbegul N, Dede O, Daggulli M, Hatipoglu N, Bozkurt Y. A novel percutaneous nephrolithotomy (PCNL) set: The 'Economical One-shot PCNL Set' (Ecoset). Arab Journal of Urology. 2017;15(3):199-203.
13. Peng P, Lai S, Ding Z, et al. One-shot dilation versus serial dilation technique for access in percutaneous nephrolithotomy: a systematic review and meta-analysis. BMJ Open 2019;9:e025871.
14. Chiancone F, Meccariello C, Fedelini M, Giannella R, Fedelini P. Four dilation techniques in percutaneous nephrolithotomy: a single-institute comparative analysis. Minerva Urol Nephrol 2021;73:253-9.

15. Sharma A, Parab S, Goyal G, Patel A, Andankar M, Pathak H. Comparison of single-step renal dilatation and serial renal dilatation in percutaneous nephrolithotomy: A retrospective case–control study. Urol Ann 2021; 13:374-7
16. Girisha TD, Dev P, Vijaykumar R, Dharwadkar S, Madappa KM. Single-step dilatation in percutaneous nephrolithotomy, its safety and efficacy: A prospective, single-center study. Urol Ann. 2019;11(2):171-174.
17. Suelozgen T, Isoglu CS, Turk H, Yoldas M, Karabicak M, Ergani B, Boyacioglu H, Ilbey YO. Can We Use Single-step Dilation as a Safe Alternative Dilation Method in Percutaneous Nephrolithotomy? Urology. 2017 Jan;99:38-41.
18. Srivastava A, Yadav KK,Singh A, et al. Feasibility of one-shot dilation access in the pediatric age group. World Jnl Ped Surgery 2022;5:e000311.
19. Acharya, GB., Shrestha, A., KC, H., Basnet, R., Shah, A., & Shrestha, P. (2017). Randomized study comparing safety and efficacy of one shot versus serial metal telescopic dilation technique in percutaneous nephrolithotomy. Journal of Society of Surgeons of Nepal, 20(2), 13-19.
20. Mohyelden, K., Abdel-Rassoul, M., Dogha, M., Kadry, A. and Mostafa, A., 2021. One-shot dilatation versus metal dilator during percutaneous nephrolithotomy in Flank-free supine position: A Randomized Controlled Study. Journal of Endourology,.
21. Arslan E, Türk H, Öğütlü A, Ün S. The Effect of One-shot Multi-access Percutaneous Nephrolithotomy on Complications. Journal of Urological Surgery. 2019; 6(1): 16-20.

Authors Contribution

HKW: Conceptualization of Project
AA: Data Collection
TAW: Literature Search
MRG: Statistical Analysis
AA, SHS: Drafting, Revision
MN, GJAN: Writing of Manuscript

Severity of Rheumatoid Arthritis, and Levels of Vitamin D3 & C-Reactive Protein

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Abstract

Objective: Study was designed to assess the severity of rheumatoid arthritis, with level of vitamin D and C-reactive protein in a group of patients.

Method: This study was conducted at Govt Kot Khawaja Saeed Teaching Hospital. Duration of study was from June 2017 to June 2018. This cross sectional study was carried out on 50 consented patients with Rheumatoid arthritis fulfills the criteria of 2010 Rheumatoid arthritis classification. Both genders with age range 18-60 year were included in the study. Patients/controls were comprised as group 1(25 patients with mild type arthritis),group 2(25 patients with moderate form of arthritis) and group 3 (healthy controls).

Results: It is observed that most of the patients of group2 have small joint involvement with severe to moderate pain /swelling as compared to group 1. Mean difference /standard error of vitamin D and C-reactive protein among group 1 and group 2 were significantly higher as compared to controls.

Conclusion: Study found significant deficiency of vitamin D along with high values of C-reactive protein in patients with severity of arthritis.

Keywords: Rheumatoid Arthritis, vitamin D, C-reactive protein

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Introduction

Rheumatoid arthritis (RA) is an inflammatory agonizing disease of the synovial joints. The key characteristic of this complex autoimmune disorder is the inflammation of the small joints. It also involves different system of patients. Prevalence of RA was 26.9% in Pakistan, which shows >5% rise/ year. This showed that prevalence of RA in high in Pakistani population as compared to African, European and Japanese population.[1,2,3] RA is more prevalent in female in comparison to male gender. The chronic inflammation of synovium-part of the joint results in manifestation of several arcticular and extra-articular sits resulting in increased morbidity/ mortality. The aetiologyof RA may be based on genetic / non-genetic factors like hormonal, environmental and infectious issues.[4] Diagnosing of RA is not based to any specific test. However anti cyclic citrullinated peptide has some good specificity and may be related with severity of disease.[5] Levels of reactants of acute-phase like ESR and CRP are raised and may be relate with RA. Level of CRP greater than 3.0 mg/L is related with swollen to tender joints.[6,7]

Pathogenesis of rheumatoid arthritis shows that, it is an autoimmune, inflammatory ailment that included abnormal triggering of osteoblasts, B -cells and T- cells, fibroblasts, chondrocytes, proteolytic enzyme and dendritic cells results in injury of bone, cartilage and tendons as well as manifestation of systemic and extra-arcticular RA.[8] Due to the presence of vitamin D related receptors, vitamin D play an important role in controlling the immune / adaptive responses and boost the immune

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system, and low levels of vitamin D results autoimmunity.[9] Receptors of vitamin are also present in synoviocytes and chondrocytes. Changes in levels of circulating vitamin D may affect cellular signaling pathways resulting in many disorders particularly calcium homeostasis, metabolism of bon and dysfunction of immune system. Deficiency of vitamin D is related with various autoimmune problems including RA.[10,11] However a study found insignificant relations between the activity of rheumatoid arthritis ailment and the level of circulating vitamin D level[12]. Inadequate data are offered for finding the link of level of vitamin D3 with RA especially in country of Pakistan. Study is therefore designed to assess the severity of rheumatoid arthritis, with level of vitamin D and C-reactive protein in a group of women.

Material and Methods

A cross sectional study was carried out on 50 consented patients with Rheumatoid arthritis fulfils the criteria of classification of Rheumatoid arthritis[13]. Both male and female with age range 18-60 year were taken from Govt Kot Khawaja Saeed Teaching Hospital. Duration of study was from June 2017 to June 2018. RA was confirmed based on sign / symptoms and radiological findings on X-ray. Patients/controls were comprised as group 1(25 patients with mild arthritis), group 2(25 patients with moderate form of arthritis) and group 3 (20 age, sex matched healthy controls). The inclusion criterion was based on DAS scoring system. The patients freshly diagnosed by rheumatologist, using vitamin D supplement, or with any serious morbidity like SLE were not included in the study.

Patients were taken using consecutive convenient non-probability sampling. Letter of IRB was obtained from the Post Graduate Medical Institute. Demographic variables like age, socioeconomic status, profession and blood pressure were noted. Levels of vitamin D< 30.0 ng/ml were classified as hypo-vitaminosis D.[14]

Data was entered and analyzed by SPSS 20. Demographic variables including profession, socioeconomic status, health status and involvement of joints, swelling and severity of disease were expressed in frequency and percentages. Quantitative variables including age, blood pressure, pulse rate were expressed as mean±SD. One way Anova was used to find the significant different among patients groups and control subjects. P<0.05 showed significance.

Table 1: *Demographics of patients (group 1 and 2) and controls (group 3)*

Variables	Group 1	Group 2	Group 3
Age	36.4±10.1	37.4±10.2	32.7±11.0
Professional	12 (60%)	11(55%)	12(60%)
Non-Professional	8(40%)	9(45%)	8(40%)
Socioeconomic status			
Middle	18(90%)	18(90%)	18(90%)
Upper	2(10%)	2(10%)	2(15%)
B.P			
Systolic	129±9	132±7	132±10
diastolic	82±3	80±0	81±4

Table 2: *Clinical variables of group 1 and group 2*

Clinical variables	Group 1 Frequency and percentages	Group 11 Frequency and percentages
Small joint pain	11.0(55 %)	15(75%)
Swelling of joints	3.0 (15 %)	16(80%)
Tenderness of joints	16.0 (80 %)	0(0%)
Pain Grade		
Mild	0(0%)	19(95%)
Moderate	15(75%)	1(5%)
severe	5(25%)	0(0%)

Group 2: mild to moderate
Group 1: Moderate to severe

Results:

The Demographics of patients and control were tabulated as table 1.0. Mean age of the patient was 36 years. Majority of the patients belong to middle class and professional. All of the patients are normotensive.

Clinical variable s of patients and controls were tabulated

Table 3: *Group based comparison of vitamin D and C-reactive protein Values for patients among three study groups*

Groups (I)	Groups J	Mean Difference 1-J (vitamin D)	Standard Error	Mean Difference I-J (C-RP)	Standard Error	p- value
Group1	Group 2	32.75	3.37	-0.94	0.12	<0.001
Group1	Group 3	49.30	3.37	-2.71	0.12	<0.001
Group 2	Group 3	16.55	3.37	-1.77	0.12	<0.001

as table 2. It is observed that most of the patients of group 2 have small joint involvement with profound swelling. However, the tenderness and pain is mostly observed in group 1. In group 1 the status of aching is higher as compared to group 2. In group 1 aching status is moderate to severe as compared to group 2.

Group wise comparison of vitamin D3 and CR-P values among patients and controls was tabulated as table 3. By using One way ANOVAs, it is observed that mean difference /standard error of vitamin D and C-reactive protein among group 1 and group 2 was significantly higher ($P<0.001$) as compared to control group 3. Conversely, the mean difference / standard error of vitamin D and C-reactive protein among group 2 was higher significantly ($P < 0.001$) in comparison with controls.

Discussion

We observed that majority of the patients with age group 33 to 36 years belong to middle class, female and professional. All of the patients are normotensive. A study found that age group of RA patients was 44.0 years and belong to middle class with nominal income and the adverse outcome is the patients cannot afford expensive treatment of RA.[15] Studies reported RA is more common in female as compared to male. The reason may be that women face social penalties, including incapability to perform house hold services and decreased ability to do work as well as outdoor activities.[16,17] This may affect their exposure to sun which is best wad of getting vitamin D. Additional lack of vitamin D may worse RA.[18]

Patients with mild to moderate form of rheumatoid arthritis have small joint involvement, joint pain with profound swelling. However, the tenderness and pain is mostly observed in patients with moderate to severe form of arthritis. They also have high status of pain as compared to patients who have mild to moderate form of arthritis. A study was conducted to find out that concentrated management is appreciated to remission of disease in patients with moderately active form of rheumatoid arthritis. It is suggested that good management is based on monthly appointments, treatment based on counselling techniques, Medicines optimization, providing handbook to patient and shared planning of treatment.[19]

Group wise comparison of vitamin D and C-reactive protein levels among patients and controls showed that mean difference /standard error of vitamin D and C-reactive protein among patients with mild to moderate and in patients with moderate to severe form of rheumatoid arthritis was significantly higher as compared to control. Study also observed that among patients with moderate to severe form of arthritis the significantly low levels of vitamin D and high values of CRP as compared to patients with mild to moderate form of rheumatoid arthritis

A study was carried out in 100 Indian RA patients and found significant deficiency of vitamin D as compared to controls. Study also found level of CRP is positively and significantly correlated with severity of disease. However, deficiency of vitamin D is common in RA patients.[20]

A study was conducted in 102 RA patients living in Saudi Arabia. Their level of vitamin D3 was estimated. It is reported that circulating values of vitamin D< 20.0 ng/mL was defined as patient to vitamin D. Results of ROC curves showed that vitamin D<12.3 ng/mL forecast high RA disease activity, and vitamin D >17.90 ng/mL forecast mild form of RA. Study reported that vitamin D is a good predictor of ailment of RA Saudi Arabian patients.[21]

A total of 377 Chines patients with RA were divided into two groups i.e. group with normal level of Vitamin D and the group low values of vitamin D. Supplements of vitamin D was given for twenty-four months to the group of patients who have low level of vitamin D. The patients were followed and record the status of pain and swelling of joints of the patients. Additionally, the levels of C-reactive protein were estimated to judge the reappearance of RA based on disease activity. Study found that vitamin D as supplement may improve the sign and symptoms of disease. However, reduced values of vitamin D increase the risk of reappearance of RA.[22]

A study carried out in 42 Indian RA patients and estimates their DAS score, levels of CRP and vitamin D. Study found that deficiency of vitamin in RA patients was inversely correlate with DAS score/tenderness of joint and CRP. It is reported that each increase of dose of 10.0ng/ ml of vitamin D is related with reduction in the severity of disease and reduce 25 % CRP.[23] A study confirmed the immunomodulatory function of vitamin D3 besides its traditional role of controlling the metabolism of calcium and phosphorus in body.[24] Another study carried out in 790 patients living in UK and recorded their baseline demographic characteristics, duration of sign and symptoms, stiffness in morning,

fatigue, counts of swollen and tender joint counts and DAS score. Study found no apparent link between values of serum vitamin D and baseline characteristic, activity of disease of RA or progression from arthritis or arthralgia to RA.[25]

Limitations of study: Study was carried out in only one hospital. Sample size was small. Future studies are needed to take the patients form different hospitals that may confirm the results of this study. Additionally, there is a need to assess the doses of supplementation of vitamin D to find better treatment Moreover, studies assessing the dosage of vitamin D supplementation are also required to explore better treatment tactics.

Conclusions

Study found significant deficiency of vitamin D along with high values of C-reactive protein in patients with severity of arthritis. Supplementation of vitamin D3 may be needed for reducing the severity of the ailment. Screening of RA patients for finding the levels of vitamin D is needed. The treatment cost of RA is high and not correlated with the financial status of people. There is a need that Pharmacists should guide patients and aware patients about ailment and strictly use the medicine.

References

1. Zlatković-Švenda MI, Stojanović RM, B Šipetić-Grujičić S, Guillemin F. Prevalence of rheumatoid arthritis in Serbia. Rheumatol Int. 2014;34:649-58.
2. Rossini M, Rossi E, Bernardi D, Viapiana O, Gatti D, Idolazzi L, et al. Prevalence and incidence of rheumatoid arthritis in Italy. Rheumatol Int. 2014;34:659-64
3. Yamanaka H, SugiyamaN, InoueE, TaniguchiA, MomoharaS.Estimates of the prevalence of and current treatment practices for rheumatoid arthritis in Japan using reimbursement data from health insurance societies and the IORRA cohort (I). Mod Rheumatol. 2014; 24:33-40
4. Frank-Bertonecelj M, Klein K, Gay S. Interplay between genetic and epigenetic mechanisms in Rheumatoid Arthritis.Epigenomics 2017;9:493-504
5. Bizzaro N, Bartoloni E, Morozzi G, Manganelli S, Riccieri V, Sabatini P, et al. Anti-cyclic citrullinated peptide antibody titer predicts time to rheumatoid arthritis onset in patients with undifferentiated arthritis: results from a 2-year prospective study. Arthritis Res Ther. 2013;15(1):R16.
6. Kotulska A, Kopeć-Mędrek M, Grosicka A, Kubicka M, Kucharz EJ. Correlation between erythrocyte sedimentation rate and C-reactive protein level in patients with rheumatic diseases. Reumatologia. 2015;53(5):243-246.
7. Graf J, Scherzer R, Grunfeld C, Imboden J. Levels of C-Reactive Protein Associated with High and Very High Cardiovascular Risk Are Prevalent in Patients with Rheumatoid Arthritis. PLoS ONE 2009;4(7): e6242.
8. Smolen JS, Aletaha D, Barton A, Burmester GR, Emery P, Firestein GS, et al. Rheumatoid Arthritis. Nat Rev Dis Primers 2018: 4:18001.
9. Aranow C. Vitamin D and the immune system . J Investig Med. 2011, 59:881-6.
10. Habib AM, Nagi K, Thillaiappan NB, Sukumaran V and Akhtar S. Vitamin D and Its Potential Interplay With Pain Signaling Pathways. Front. Immunol 2020; 11: 820.
11. Muhammad MA , John P, Bhatti A, Jahangir S, Kamboh MI. Vitamin D as a Principal Factor in Mediating Rheumatoid Arthritis-Derived Immune Response. BioMed Res Int; Volume 2019, Article ID 3494937, 12 pages
12. de la Torre Lossa P, Moreno Álvarez M, González Guzmán MC, LópezMartínez R, Ríos Acosta C. La vitamina D no esútilcomo biomarca dorpara la actividad de laenfermedad en arthritis reumatoide. Reumatol Clin. 2020;16:110–115.
13. Kay J, Upchurch KS., ACR/EULAR 2010 rheumatoid arthritis classification criteria, Rheumatology 2012; 51 (suppl_6): vi5–vi9
14. Atwa MA, Balata MG, Hussein AM, Abdelrahman NI, Elminshawy HH. Serum 25-hydroxyvitamin D concentration in patients with psoriasis and rheumatoid arthritis and its association with disease activity and serum tumor necrosis factor-alpha. Saudi Med J. 2013 Aug;34(8):806-13.
15. Naqvi AA, Mohamed AH, Mohammad TA. Epidemiology of rheumatoid arthritis, clinical aspects and socioeconomic determinants in Pakistani patients: A systematic review and meta-analysis. JPMA 2019; 69(3): 389-398
16. Naz S, Aslam R, Ehsan-ullah, Shahzad F, Mushtaq A, Ahmad TM, et al. Association of erythrocyte sedimentation rate and c-reactive proteins with active disease in juvenile rheumatoid arthritis. Pak Paed J. 2014; 38: 24-30.
17. Kłak A, Raciborski F, Samel-Kowalik P. Social implications of rheumatic diseases. Reumatologia. 2016; 54:73-8
18. Sukharani N , Dev K , Rahul F , Bai P , Ali A , Avinash F et al. Association Between Rheumatoid Arthritis and Serum Vitamin D Levels. Cureus 2021; 13(9): e18255.

19. Prothero, L., Sturt, J., de Souza, S. Lempp H. Intensive management for moderate rheumatoid arthritis: a qualitative study of patients' and practitioners' views. BMC Rheumatol 2019;3(12):2-11.
20. Kumar R, Kunal K, Kumar N. Vitamin D in rheumatoid arthritis and association of disease activity with various laboratory parameters. J Orthop Dis Tarumatol 2021; 2: 21-5
21. Azzeh FS and Kensara OA. Vitamin D Is a Good Marker for Disease Activity of Rheumatoid Arthritis Disease . Disease Markers Volume 2015. 6 pages
22. Borukar SC, Chogle AR, Deo SS. Relationship between Serum 25-Hydroxyvitamin D Levels, Disease Activity and Anti-Cyclic Citrullinated Peptide Antibody Levels in Indian Rheumatoid Arthritis Patients. J Rheum Dis Treat 2017; 3:056.
23. Patel S, Farragher T, Berry J, Bunn D, Silman A and Symmons D: Association between serum vitamin D metabolite levels and disease activity in patients with early inflammatory polyarthritis. Arthritis Rheum. 2007; 56:2143–2149.
24. Rehan MA. Umber AJ, Khan MR, Azeem W, Aftab H, Anjum A et al. Immunomodulatory role of vitamin D in infectious and non-infectious diseases. Hosts and Viruses 2019; 6(5): 115-129.
25. Harrison SR, Jutley G, Li D, Sahbudin I, Filer A, Hewison M et al. Vitamin D and early rheumatoid arthritis. BMC Rheumatol 2020;4:38

Authors Contribution

MH: Conceptualization of Project
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HH: Literature Search
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GR: Drafting, Revision
FA: Writing of Manuscript
S.S.U: Literature Review

The Spectrum of Central Nervous System Tumours at the Tertiary Care Hospital: A Three Year Study

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Abstract

Objective: To study the spectrum of central nervous system in our local population in a tertiary care hospital.

Method: This study was set in King Edward Medical University Pathology laboratory for a period of three years. All the CNS tumors sent to the histopathology department and reported were included in this study after following a strict criterion of inclusion and exclusion. A total of 110 cases were included in this study. All the cases were reviewed by 2 separate histopathologists. Data was collected using pre-designed proforma used in the laboratory which covers various aspects of the processes involved from specimen requisition till dispatch of final report. Data collected was entered by using Statistical package for social sciences (SPSS version 21).

Results: Majority of cases were categorized in the benign category and Meningioma was seen as the most common tumour. The age group most commonly observed was 40-60years of age and there was no difference in incidence between the gender. Glioblastoma was the most common malignant tumor noted.

Conclusion: This study gives a good overall picture of the spectrum of CNS tumors in local population. Their incidence needs to be investigated and documented so that a proper idea of their prevalence can be made in order to benefit the patients and clinicians alike.

Keywords: Central nervous system, tumours, Meningioma, Brain.

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Introduction

Tumours of the central nervous system are cause of a significant amount of morbidity and mortality worldwide. Their incidence is much higher in continents like Europe, Australia and North America as compared to Asia, South East Asia and India.[1] Although these tumours are rare, the extent of morbidity and mortality caused is not in proportion to their incidence. According to cancer statistic 2016 in United States CNS tumours accounted to 1.4 percent of new cancers reported and 2.7 percent of deaths resulting from cancer.[2] In the UK approximately 9000 people are diagnosed with primary CNS tumours each year[3] and estimated death toll is 3 percent of the total cancer deaths. There has been a sharp rise in their incidence up to 39% from early 1990s to 2018.[4] Unfortunately, there have been only a handful of studies done in Pakistan regarding the incidence of brain tumours and more research is needed to find out the ongoing trend of these tumours. Cancer in general is on the rise in our country and looking into the occurrence of various tumours in our general population gives us a good idea to establish better guidelines regarding their management. The incidence of CNS tumours according to a 10year study in Pakistan is 1.2 percent.[5] In order to have a more updated data, in this study 3 years of data from a tertiary care hospital in Punjab has been compiled to get a fresh look at the spectrum of CNS tumours in local population.

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Material and Methods

This cross sectional study was done at Histopathology laboratory of King Edward Medical University. The 3 years data of total 110 patients both males and females was categorized according to age into the following categories: less than 10 years(yrs),10-20 yrs,20-40 yrs, 40-60 yrs and greater than 60 yrs. The site of origin of the tumour was specified as following: brain, spinal cord, orbit and extradural. The tumours were then divided into 2 categories of benign and malignant. All the histopathology reports of the cases from 1st January 2016 - 31st December 2018 were reviewed in the study. Histopathological diagnosis, tumour site, age and gender of the patients were noted. Histological examination was carried out by a consultant histopathologist under light microscope. Data was collected using pre-designed proforma used in the laboratory which covers various aspects of the processes involved from specimen requisition till dispatch of final report. Reports of patients with autolyzed, unremarkable diagnosis and differential diagnosis were excluded from this study. Only cases with agreed upon single diagnosis were included to avoid discrepancy. Data collected was entered by using Statistical package for social sciences (SPSS version 21). Pearson Chi Square test was performed to see association between different variables and p value less than 0.05 was taken as significant.

Results

A total of 114 cases were studied. Out of these cases, 1 was reported as unremarkable brain parenchyma, 2 reported with a list of differential diagnosis with no agreed upon diagnosis and one specimen was reported as autolyzed. These were excluded from the count. Finally, 110 cases were included in the study. There was a wide age range in the cases received at the pathology department, ranging from less than 10 year to 60 years and greater. Most affected age group seen was 40-60 years. The least affected group was less than 10 years of age. The incidence in males and females was the same. The male to female ratio was 1:1. The number of benign CNS tumours was 65(59%) and that of malignant tumours was 45 (41%) in total. The frequency of benign tumours was more in females (61%) as compared to malignant, which were more common in males (60% of all the malignant tumours). The distribution of benign and malignant tumours in different age groups is given in Figure 1. Most common age group for malignancy and benign tumours was 40-60 years. However, no association between age groups and nature of tumour i.e. benign and malignant was observed after application of Pearson Chi Square (p value=1.0). The least amount of malignancy was seen in less than 10 years of age (n=0). The most common tumour overall regardless of age and gender was found to be Grade I Meningioma (46 cases) followed by Grade II Astrocytoma and Glioblastoma (12 and 11 cases respectively). According to the nature of origin, the number of primary CNS tumours was 102 and of metastatic tumours including atypical lymphoproliferative tumours and others for example plasmacytoma, pleomorphic adenoma and hemangioma was 8. The incidence according to the originating site, tumours originating from brain parenchyma (n=85) was the most common site of primary CNS tumours, followed by the spinal cord (n=20), extradural (n=3) and orbit (n=2). The detailed spectrum of the most common tumours in this study (meningeal origin) is given in Table1. Comprehensive range of all tumours is given in Table 2.

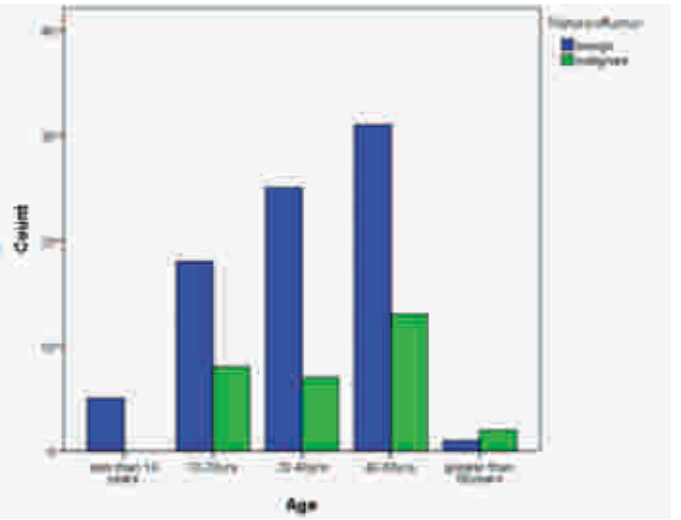

Fig-1. *Graph representing the various age groups of benign and malignant CNS tumours.*

Table 1: *Spectrum of Meningioma, the most common tumour found in this study (n=54).*

Tumour Type	Tumours Grade	Number	Percentage	Age Range(yrs) (most common)	Male	Female	Ratio M;F
Meningioma	I	46	85.3%	40-60	15	31	1:2
Atypical Meningioma	II	5	9.2%	20-40	4	1	4:1
Anaplastic meningioma	III	3	5.5%	40-60	1	2	1:2

Table 2: *Comprehensive details of all the tumours found in this study (n=110).*

Tumour Type	Tumour grade	Number	Percentage (%)	Age range < 18 yrs	Age range >18 yrs	Male	Female	Commonest Location
Meningioma	I	46	41.8	14	32	15	31	Brain and spinal cord
Atypical meningioma	II	5	4.5	1	3	4	1	Brain
Anaplastic meningioma	III	3	2.7	1	2	1	2	Brain
Glioblastoma	IV	11	10	0	11	6	5	Brain cerebral
Atypical Astrocytoma	II	12	10.9	3	9	10	2	Brain cerebral
Anaplastic Astrocytoma	III	4	3.6	2	2	3	1	Brain cerebral
Pilocytic Astrocytoma	I	3	2.7	3	0	1	2	Third ventricle
Diffuse Glioma	I	1	0.9	0	1	1	0	Brain cerebral
Oligodendroglioma	II	3	2.7	0	1	2	1	Brain cerebral
Ependymoma	I	2	1.8	1	1	2	0	Spinal cord
Shwanoma	-	3	2.7	2	1	2	1	Spinal cord, orbit
Pituitary adenoma	-	4	3.6	0	4	3	1	suprasellar
Encephalocoel	-	1	0.9	1	0	0	1	Spinal cord
Round blue cell tumour	-	1	0.9	1	0	1	0	Spinal cord
Hemangioma	-	1	0.9	0	1	1	0	Spinal cord
Atypical Lymphoproliferative	-	2	0.9	0	2	0	2	Spinal cord
Pleomorphic adenoma	-	1	0.9	0	1	0	1	orbit
Dermoid cyst	-	1	0.9	0	1	1	0	Posterior fossa
Craniopharyngioma	I	2	1.8	1	1	0	2	Suprasellar
Plasmacytoma		1	0.9	0	1	0	1	Extra dural
Metastatic tumour	-	3	2.7	0	3	2	1	Brain cerebral and extra dural

Discussion

Cancer data on brain and nervous system tumours reported in Pakistan is not widely studied and the variety of tumours found in our local population has not been reported in detail. There are a handful of studies conducted in this area and this study is an attempt to add to the collective data for future research and generate comprehensive information so these patients can be effectively treated and required resources can be made available to this category of neoplasms.

In this study, the most common CNS tumour encountered was Meningioma followed by Astrocytoma and then Glioblastoma which is similar to a study in Bangladesh.[6,7] While in a study in India Astrocytoma was the most common tumour found which coincides with incidence in England as well.[8,9] There was a no difference in incidence seen between males and females, however a slight male predominance has been reported in other studies.[6-8]

In this study the most common age group was 40-60, which is in accordance to an age standardized related incidence study of cancer done in Pakistan[(10)], the incidence of brain and nervous system tumours was found predominant in males than females which has not been validated by our study. Ependymoma was the most common tumour seen in a study conducted on pediatric population however our observation shows that Meningioma was most common in the pedia-tric (less than 18 yrs) population.[11] Studies performed on pediatric population in other parts of the world also showed a varied picture where some found astrocytoma as the most common tumour while others found medulloblastoma.[6-8] A study done in Pakistan showed that most brain surgeries are performed in private setup and not in Government owned facilities like the hospital where this study was conducted so there is a factor of population understudy that might cause the variation in the data and might not show a full picture of the prevalence of these tumors.[12] Which may explain why another study done in a private Hospital in Karachi, Pakistan showed diffuse glioma as the most common but age range and location was similar to our data.[13] Our findings, however match a Chinese study which reports meningioma is

the most common tumour observed as well.[14] A Korean study also mirrors our results with meningioma being the most common tumour reported out of a large number of cases studied. However, they noted a female predo-minance in their observations. Similar to our data Glio-blastoma was reported as the most common malignant tumour.[15]

By examining a wide variety of studies on CNS tumours, it seems that there is still a need to explore their spectrum in our population to reach a definite conclusion. This study is an attempt in this direction.

Conclusion

Central nervous system tumors impose a long-lasting influence on the health of the patients and also inflict burden on the health care system. In our setup benign tumours are found to be most common. Meningioma (grade I) is the most widely encountered tumour, followed by Atrocytoma (grade II) and Glioblastoma. Interestingly Meningioma (grade I) was also the commonest among patients aged less than 18 years. This study has evaluated the prevalence of CNS tumours in local population in order to help health care professionals and authorities get a better idea of its spectrum and help devise further action plans for future.

Conflict of Interest. None

References

1. Leece R, Xu J, Ostrom QT, Chen Y, Kruchko C, Barnholtz-Sloan JS. Global incidence of malignant brain and other central nervous system tumors by histology, 2003-2007. Neuro Oncol. 2017;19(11):1553-64.
2. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2016. CA: A Cancer Journal for Clinicians. 2016;66(1):7-30.
3. Kurian KM, Jenkinson MD, Brennan PM, Grant R, Jefferies S, Rooney AG, et al. Brain tumor research in the United Kingdom: current perspective and future challenges. A strategy document from the NCRI Brain Tumor CSG. Neuro-Oncology Practice. 2017; 5(1): 10-7.
4. CancerResearchUK. Brain, other CNS and intracranial tumours incidence statistics [website]. 2021 [cited 2021 11 November]. Available from: https://www. cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/brain-other-cns-and-intracranial-tumours/incidence
5. Jamal S, Moghal S, Mamoon N, Mushtaq S, Luqman M, Anwar M. The pattern of malignant tumours: tumour registry data analysis, AFIP, Rawalpindi, Pakistan (1992-2001). JPMA The Journal of the Pakistan Medical Association. 2006;56(8):359-62.
6. Begum SKN, Parvez M, Hoque MR, Khan O, Barua RR, Sultana S. Spectrum of Central Nervous System Tumours in a Tertiary Hospital of Bangladesh. Journal of Medicine. 2019;20(1):34-7.
7. Pouchieu C, Gruber A, Berteaud E, Ménégon P, Monteil P, Huchet A, et al. Increasing incidence of central nervous system (CNS) tumors (2000–2012): findings from a population based registry in Gironde (France). BMC cancer. 2018;18(1):653.
8. Shah M, Jain SIDB. Distribution of various CNS tumors in a tertiary care hospital: Ten year retrospective study. IJAR. 2018;4(4):192-5.
9. Arora RS, Alston RD, Eden TO, Estlin EJ, Moran A, Birch JM. Age–incidence patterns of primary CNS tumors in children, adolescents, and adults in England. Neuro-oncology. 2009;11(4):403-13.
10. Badar F, Mahmood S. Cancer in Lahore, Pakistan, 2010-2019: an incidence study. BMJ open. 2021; 11(8): e047049.
11. Qurni M, Tariq, H., Tahir, H., Din, H., Mansur, H. and Nadeem, M. . Frequency of pediatric brain tumors in tertiary care institute of pakistan and comparison with international data. PAFMJ. 2021;71(3):p992-5.
12. Baig E, Shah M, Bajwa MH, Laghari AA, Akhunzada NZ, Bin-Anis S, et al. Conducting a nationwide brain tumor epidemiology study in an LMIC: A multi-institutional experience. Neuro Oncol. 2021;23(Suppl 6):vi89 - vi90.
13. Danish F, Salam H, Qureshi MA, Nouman M. Comparative clinical and epidemiological study of central nervous system tumors in Pakistan and global database. Interdisciplinary Neurosurgery. 2021;25:101239.
14. Chen L, Zou X, Wang Y, Mao Y, Zhou L. Central nervous system tumors: a single center pathology review of 34, 140 cases over 60 years. BMC Clinical Pathology. 2013;13(1):14.
15. Lee CH, Jung KW, Yoo H, Park S, Lee SH. Epidemiology of primary brain and central nervous system tumors in Korea. Journal of Korean Neurosurgical Society. 2010;48(2):145-52.

Authors Contribution

MA: Conceptualization of Project
SS: Data Collection
SA: Literature Search
MK: Drafting, Revision
MK: Writing of Manuscript

Role of Oral Progesterone in Pre Term Labour

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Abstract

Objective: Our study aims at determining safety and efficacy of oral micronized progesterone in preventing preterm labor.

Method: Study conducted at Sahiwal Teaching Hospital from June 2018-July 2019 including 180 participants with preterm labor. Oral micronized progesterone give 200 microgram twice daily till preterm labor settled.

Results: 12.5% were ⩽ 20 years. 31% were 20-25 years. 35% were from 25-30 years. While 36(22%) were ⩾ 35 years. Primigravida were 27% and multigravida 73%. In 76% cases preterm labor settled and 24% had labor ⩽ 37 weeks. Latency period ⩽ 24 hours in 15% ,2-6 days in 18%, 1-3 weeks in 24%, 4-8 weeks in 32%, 9-12 weeks in 7%, ⩾ 12 weeks in 5% respectively. 78% had vaginal delivery, C-Sec in 22% of patients. Gestational age at delivery ⩽ 28 weeks in 7%, ⩽ 32 weeks in 20%, ⩽ 36 weeks in 25% and ⩾ 37 weeks in 48% respectively. Birth weight, ⩾ 3.0 kg in 25%, 2.0-2.5 kg in 50%, ⩽ 2.0 kg 18%, ⩽ 1.5 kg 7%. NICU admission 25%. RDS seen in (22%), Sepsis (10%), IVH (3%), NEC (1%). neonatal deaths were 12.

Conclusion: Oral micronized progesterone is found to be safe, effective and well tolerated therapy for prevention and treatment of preterm birth.

Keywords: Progesterone, Preterm birth, latency period

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Introduction

Globally 3 in 4 neonatal deaths occur due to preterm births complications. Incidence of neonatal mortality due to preterm birth is 28%. Annually about fifteen million babies are born before 37 weeks of pregnancy. That is more than 1 in 10 babies. Approximately one million children die due to complications of preterm. Global prevalence of preterm birth is 9.6%, in Pakistan 15.7% whereas in Australia it is 6.6%. Preterm birth is one of major contributor to infant mortality and morbidity.[1,2]

Preterm birth is defined as birth of baby before 37 completed weeks of pregnancy. Preterm labor is further divided into late preterm (35-36 weeks), moderately preterm (32-34 weeks), early preterm (28-31 weeks) and severely preterm (28 weeks). It accounts for more than 50% neurological disabilities. Complications include respiratory distress syndrome, retrolental fibroplasias, necrotizing enterocolitis, cerebral palsy and learning disabilities. All these complications lead to increase in neonatal and child mortality less than five years.[3,4]

Preterm birth is a considerable source of financial burden on government and families. In developing countries situation is even graver due to lack of provision of neonatal facilities and services uniformly all over the country. Although remarkable changes are being made in public sector but there is a lot to do more as burden

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of prematurity is considerably high in Pakistan.[1,5]

A lot of interventions have been made to decrease the incidence of preterm labor. Amongst these progesterone seems to be most promising, easy to administer and cost effective with high safety profile. Progesterone has a pivotal role in containing pregnancy till term due to its anti-inflammatory role. American college of Obstetrician and Gynecologists recommended progesterone as a prophylaxis to prevent preterm labor in women with previous preterm labor and short cervical length.[6,7,8]

Role of progesterone in preventing preterm labor was characterized in 1934 and first reported in literature in 1954. Since then a lot of research is going on different routes and preparation of progesterone including vaginal, intramuscular and oral rotes. Different formulations available are 17 hydroxy progesterone, dydrogesterone and oral micronized progesterone.[8,9]

A lot of research available on vaginal progesterone though it was associated with difficulty in administration and unpleasant vaginal discharge. Oral progesterone was studied first in preventing preterm labor but lagged behind in research. It was not due to decreased efficacy of oral progesterone but rather lack of preference of oral progesterone by researching bodies. Even in Pakistan there is scarcity of research in role of oral micronized progesterone preventing preterm birth.[10]

Material and Methods

This study was conducted at Sahiwal teaching hospital Sahiwal for a period of one year from June 2018 till June 2019. It was quasi experimental study. 180 women participated in study after informed consent and fulfilling inclusion criteria. Preterm labor was defined as onset of regular uterine contractions at least 3 in 10 minutes for 20-25 seconds (between 24-36+6 weeks). All patients underwent detailed history and examination. Sterile speculum and pelvic examination done to assess cervical changes and dilatation. Patients having premature contractions given oral micronized progesterone 200 mg twice a day till labor settled and discharged to home. Treatment continued till 36 weeks and patients were called on regular follow up visits. At each visit patients were assessed for signs and symptoms of labor and any complications related to progesterone treatment including headache, nausea, vomiting, constipation and dizziness. During course of study 18 patients lost follow up so at end of study there were total 162 participants.

Inclusion criteria: All women with single preterm labor from 24 weeks till 36+6 weeks.

Exclusion criteria:

- Multiple pregnancies
- Thromboembolic disease current or history
- Breast /genital tract malignancy
- Presence of fever or sepsis
- Heavy vaginal bleeding requiring surgical intervention
- Active labor (Cervical dilatation 4cm)

Results

12.5% were years. 31% were 20-25 years. 35% were from 25-30 years. While 36(22%) were 35 years. Primigravida were 27% and multigravida 73%. In 76% cases preterm labor settled and 24% had labor 37 weeks. Latency period 24 hours in 15% ,2-6 days in 18% , 1-3 weeks in 24%, 4-8 weeks in 32%, 9-12 weeks in 7%, 12 weeks in 5% respectively. 78% had vaginal delivery, C-Sec in 22% of patients. Gestational age at delivery 28 weeks in 7%, 32 weeks in 20%, 36 weeks in 25% and 37 weeks in 48% respectively. Birth weight, 3.0 kg in 25%, 2.0-2.5 kg in 50%, 2.0 kg 18%, 1.5 kg 7%. NICU admission 25%. RDS seen in (22%), Sepsis (10%), IVH (3%), NEC (1%) neonatal deaths were 12.

Discussion

More than 60% of births occur in Africa and South Asia, but preterm birth is truly a global problem. In the lower

Table 1: *Maternal Characteristics*

Characteristics	N=162	%
Age		
⩽20 years	20	12
20-25 years	50	31
26-30 years	56	35
⩾ 30 years	36	22 (mean=27±8)
Gravidity		
Primigravida	44	27
Multigravida	112	73
History of preterm labor		
Yes	30	18
No	132	82
BMI		
25-30	150	93
⩾ 30	12	7

Table 2: *Obstetrical outcome*

Outcome	N=162	%
Preterm labor		
Settled	124	76
Not settled	38	24
Tocolysis to delivery interval		
⩽1 day(24 hours)	24	15
2-6days	28	18
1-3 weeks	38	24
4-8 weeks	52	32
9-12weeks	12	7
⩾12 week	8	5
Meconium staining of liquor	40	25
Mode of delivery		
SVD	126	78
Cesarean section	36	22
Gestational age at delivery	N=162	%
⩽28 weeks	13	7
28-32 weeks	31	20
33-36 weeks	40	25
⩾37 weeks	78	48

Table 3: *Neonatal outcome*

Characteristics	N=162	%
Birth weight(Kg)		
⩽1.5	12	7
1.5-2.0	30	18
2.0-3.0	80	50
⩾3.0	40	25
APGAR Score ⩽7	42	26
At 1min	10	6
At 5 min	110	68
APGAR Score ⩾7		
Neonatal complications	58/162	36
RDS		
IVH		
NEC		
Sepsis		
NICU Admissions	40	25
Neonatal deaths	12	7.5

income countries, on average 12% of babies are born too early compared with 9% in higher income countries. Pakistan is at 4th number in having preterm births. There is a dramatic difference in survival of premature babies in developed and underdeveloped countries. About 90% of babies born at 28 weeks die in low income countries and only 10% of babies born at this gestation die in developed and high income countries. Each day 600 newborn die due to complications related to birth asphyxia, prematurity and sepsis (UNICEF).[1,11]

Progesterone is a key factor in controlling preterm birth. The first and foremost study on role of oral micronized progesterone in a multicentre RCT including 57 patients. Our study showed the efficacy of oral progesterone in treatment of preterm labor. Research conducted in our department showed mean age of patients was 27±8. In other National and international studies mean age was relatively high and was around 29-30±6. It showed that teen age pregnancies contributed to preterm labor in our study.[8,9,12]

Most of patients presenting to sahiwal teaching hospital gynae department were multigravida about 2/3rd (67%) while 1/3rd (33%) were Primigravida. While RCT conducted at Bangkok hospital showed number of Primigravida presenting with preterm labor were more than multigravida. Gestational age range in our study was 24-36 weeks contrary to research carried out by cheung et al where pregnancy between 14-23 weeks were also included and they included cervical cerclage in patients presenting with short cervical length (⩽2.5cm).[13,14]

Regarding BMI 150(93%) women had BMI less than 30Kg/m^2 and only 12(7%) had BMI more than 30kg/m^2. In contrary to study carried out at Nishter hospital where obesity was found in 24% of population. Meis et al showed that mean BMI in patients was 26±7, which is also contradictory to our statistics. It showed that obesity was not a risk factor for patients presented to our setup.[15,16]

Progesterone showed promising results in controlling preterm births in our study, about (124) 76% preterm labors settled and only (38) 24% deliver preterm. Some national and international studies showed efficacy of progesterone in controlling preterm labor ranging from 61-68%. Ibraheem et al and Ahmad et al showed efficacy of about 64% and 68% respectively.[17,18] Rai et al showed 61% efficacy in controlling preterm labor. High success rate in our study may be due to the fact that previous history of preterm labor was in less than 20% of patients. Whereas in other studies patients with history of recurrent preterm labor were recruited in studies.[19,23] Our study showed similar results in successfully controlling preterm labor to the first study carried out at France randomizing 57 patients in placebo controlled trial where 80% of pregnancies were treated successfully.[12] Regarding latency period i.e; tocolysis to delivery interval oral micronized progesterone has shown promising results at increasing the period from onset of preterm labor and delivery of fetus. Minimum interval was 6 hours and maximum interval was 13 weeks delaying

delivery. About 1/3rd of cases 52(32%) pregnancy prolonged for up to 8 weeks (2 months). In 1/4th of pregnancies having preterm labor, uterine contractions settled and pregnancy prolonged for about 3 weeks. Pregnancy prolonged for up to 24 hours and till one week in 15% and 18% cases respectively. Our study showed even more success rates as compared to national and international studies in controlling preterm labor and increasing latency period. Research conducted by international journal showed that micronized progesterone was effective to prolong latency period for about 8 weeks .24 Study carried out at PIMS Islamabad showed role of progesterone in postponing pregnancy upto 32 days.[13] In contrast to micronized progesterone randomized controlled trial including Dyderogesterone versus placebo couldn't show any significant result in prolonging pregnancy in both groups.[14]

Regarding gestational age at delivery approximately 50% (78) patients delivered at more than 37 weeks thus improving neonatal outcome.1/4th (40) pregnancies ended up in delivery between 33-36 weeks. 31(20%) delivered at gestation ranging from 28-32 weeks. A very few 13(7%) were very very preterm, that is below 28 weeks of gestation. A double blind randomized controlled trial carried out including 150 women with previous history of preterm births and oral micronized progesterone was given to one group. This trial revealed encouraging results regarding prolonging period from onset of preterm labor till delivery. It was 36 weeks in trial group as compared to below 34 weeks in placebo group. Meconium staining of liquor was seen in 40(25%) of pregnancies. It is significantly high but not mentioned in other studies. It resulted in more NICU admissions in spite of well controlled preterm labor. No significant risk factor was seen for meconium staining.[13,22]

Most promising fact about our study was that about 126(78%) patients had spontaneous vaginal delivery and only 36(22%) had cesarean section.It may be due to the fact that most of our participants (78%) were multi gravid with previous vaginal deliveries. It was Contrary to other studies where cesarean section rates were between 66-78%.[23,24,25]

Regarding gestational age at delivery nearly half of participant (48%) in our study delivered at gestation at or more than 37 weeks. One fourth (25%) delivered at 34-36 weeks, 20% at 28-32weeks and only 7% delivered at less than 28 weeks gestation. It was comparable to studies carried out internationally and at local levels where mean gestational age at deliver was 36 weeks. In a study conducted internationally it was 35+ 2weeks. Another randomized controlled trial at America showed success rate of oral micronized progesterone in reducing preterm birth and gestational age at delivery was 37+ 2 weeks .[25,10]

As most of participants delivered beyond 36 weeks encouraging results regarding neonatal outcome seen. 50 % of neonates have birth weight ranging 2-3 kg, 25% were of more than 3 kg, low birth weight (2.0 kg) and very low birth weight (1.5 kg) were 18% and 17% respectively. It was comparable to other studies where birth weight was 2.5+0.7 kg. Admission in NICU was seen in 25% of cases. It was similar to research conducted at Hong Kong. A national study showed neonatal admissions in 5% with micronized progesterone and 22% with nifedipine. Similar results regarding neonatal admissions were seen in some international studies where neonatal admissions were 22%, but these were mostly due to very low birth weight babies. In our study most admissions were result of meconium staining of liquor. APGAR score was 7 at 1 and 5 minutes similar to other studies. Number of neonatal deaths was 12 in our study, while in other studies it was less. Increased neonatal mortality in our research was due to unavailability of optimal facilities in NICU.[16,18,22]

Very few studies are available regarding oral use of micronized progesterone most of work done on vaginal progesterone. Few randomized controlled trials were conducted at America but draw back was small number of patients so they were stopped due to failure of statistical significance. Best role of oral micronized progesterone was shown in study conducted, in which its role was observed in recurrent preterm births. This study reduced the rate of false positive results.[22]

Conclusion

Our study showed promising role of oral micronized progesterone in reducing preterm births in both spontaneous and recurrent preterm labor. Oral route was most accepted and was not associated with discomfort related to vaginal or intramuscular preparations. It was well tolerated and showed encouraging neonatal outcome.

Conflict of interest: *None*

References

1. Blencowe H, Cousens S, Ostergaard M et al. National, regional and worlwideestimates of preterm birth. The Lancet, June 2012.9;379(9832):2162-72.Estimates from 2010.

2. Beck S, Wojdyla D, Say L, Betran AP, Merialdi M, Requejo JH, et al. The worldwide incidence of preterm birth: a systematic review of maternal mortality and morbidity. Bull World Health Organ 2010; 88: 31–38.
3. Lawn J, Gravett M, Nunes T, Rubens C, Stanton C; GAPPS Review Group. Global report on preterm birth and stillbirth (1 of 7): definitions, description of the burden and opportunities to improve data. BMC Pregnancy Childbirth. 2010;10(Suppl 1):S1
4. Liu L, Oza S, Hogan D et al. Global, regional and National causes of under 5 mortality in 200-15: an updated systematic analysis with implications for the sustainable development Goals. Lancet .2016;388(10063);3027-35.
5. Asif Hanif, Tahira Ashraf et al. Prevalence of Preterm Birth in Pakistan: A Systematic Review and Meta-Analysis. ANNALS VOL 23, ISSUE 2, APR. – JUN. 2017.
6. Csapo A, Goodall M. Excitability, length tension relation and kinetics of uterine muscle contraction in relation to hormonal status.J Physiol 1954:126:384-95.Level ll-2
7. Nobolt G. Audra P et al. The use of Progesterone in treatment of menace preterm delivery.Eur J Obstet GynecolReprod Biol 1991:40:203-9.Level l.
8. American college of Obstetrician and Gynecologists. Use of Progesterone to reduce preterm birth.ACOG Committee opinion no.419. Obstet Gynecol 2008: 112: 963-5. Level lll
9. Ning A, Vladutiu CJ, Dotters-Katz SK, Goodnight WH, Manuck TA. Gestational age at initiation of 17-alpha hydroxyprogesterone caproate and recurrent preterm birth. Am J Obstet Gynecol. 2017;217:371.e1–7.
10. Sherrif Ashoushe, Osama Al kedy , Ahmad Othman. The value of oral micronized progesterone in the prevention of recurrent preterm birth: A randomized controlled trial. 2017 Nordic Federation of Societies of Obstetrics and Gynecology, Acta Obstetricia et Gynecologica Scandinavica 96 (2017) 1460–1466.
11. Vogel JP, Lee ACC, Souza JP. Maternal morbidity and preterm birth in 22 low- and middle-income countries: a secondary analysis of the WHO Global Survey dataset. BMC Preg Childbirth. 2014;14(1):1-14
12. Erny R, Pigne A, Prouvost C, Gamerre M, Malet C, Serment H, et al. The effects of oral administration of progesterone for premature labor. Am J Obstet Gynecol. 1986;154:525–9
13. Suparudeewan Thongchan and Vorapong Phupong. Oral Dydrogesterone as an adjunctive therapy in management of preterm labor: a randomized double blinded, placebo- controlled trial.BMC Pregnancy and child birth (2021)21;90.
14. Lim K, Butt K, Crane J M.SOGC . Clinical practice guide line.Ultrasonographic of cervical length assessment in predicting preterm birth in singleton pregnancies. J Obstet Gynecol Can 2011:33(5):486-99. [Practice Guide line].
15. Kizra M, Hira A. Role of oral progesterone therapy in prevention of preterm labor. Journal of Medicine, Physiology and Biophysics. ISSN-2422-8427. An International peer reviewed journal. Nol.55-2019. DOI: 10.7176/JMPB
16. Meis PJ, Klebanoff M, Thom E, Dombrowski MP, Sibai B, Moawad AH, et al. Prevention of recurrent preterm delivery by 17 alpha-hydroxyprogesterone caproate. N Engl J Med. 2003 Jun 12;348(24):2379-85. 20. Rai P, R
17. Ahmed F, Yasir S, Naeem NK, Amin A. Efficacy of 17 alpha hydroxy progesterone in prevention of preterm labour in high risk patients. Ann King Edward Med Uni. 2012;18(2):158-62.
18. Rai P, Rajaram S, Goel N, Ayalur Gopalakrishnan R, Agarwal R, Mehta S. Oral micronized progesterone for prevention of preterm birth. Int J Gynaecol Obstet. 2009 Jan;104(1):40-3. Spongy CY. Prediction and prevention of recurrent spontaneous birth. Obstet Gynecol 2007:110 (2 pt 1):405-15.
19. Eman F, Yasir S, Norah H. Use of progesterone during pregnancy to prevent preterm birth. 2020 Apr; 41(4): 333–340.doi: 10.15537/smj.2020.4.25036
20. Arikan I, Barut A. Effect of progesterone as a tocolytic and in maintenance therapy during preterm labor. Gynecol Obstet Invest. 2011:7294):269-73.
21. Borna S, Sahabi N. Progesterone for maintenance tocolytic therapy after threatened preterm labor. A randomized controlled trial. AUST NZ J Obstet Gynecol. 2008:48(1)58-63.
22. Nataranjan G, Shankaran S. Short and long term outcomes of moderate late preterm infants. Am J Perinatol. 2016:33:305-317.
23. Harrison M, Golden Berg R L.Global burden of prematurity . Semin Fetal Neonatal Med.2016:21;74-79.
24. Brien J M et al . Effect of progesterone on cervical shortening in women at risk for preterm birth: Secondary analysis from a multinational randomized double blind placebo controlled trial. Ultrasound Obstet Gynecol 2009:34:653-9.

Authors Contribution

HI: Conceptualization of Project
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ZA: Statistical Analysis
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Immune Response of Hemodialysis Patients to Hepatitis B Vaccination

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Abstract

Objective: To determine the immune response of hemodialysis patients to hepatitis B vaccination at Shaikh Zayed Hospital, Lahore.

Method: It was a cross-sectional descriptive study done at the Microbiology Department of Shaikh Zayed Hospital, Lahore after approval from the Institutional Review Board. Two hundred hepatitis B surface antigen (HBsAg) negative patients were enrolled by convenient sampling technique. Their serum samples were taken and hepatitis B surface antibody (anti-HBs) and hepatitis B core antibody (anti-HBc) were done by enzyme-linked immunosorbent assay (ELISA) technique. The data entry and analysis were done using the Statistical Package for Social Sciences (SPSS) version 25.

Results: The majority of the patients (96.5%) were vaccinated. The anti-HBs antibody was positive in 141(70.5%) patients. Out of 141(70.5%) anti-HBs positive patients, 62.5% patients had antibody titer between 10-100 IU/ml whereas only 8% patients had antibody titer of greater than 100 IU/L.

Conclusion: The anti-HBs levels were protective in 70.5% of the hemodialysis patients. The majority of the patients (62.5%) had antibody titer ranging between 10-100 IU/L and only 8% of the patients had antibody titer greater than 100 IU/L. Forty percent of patients were isolated anti-HBs positive whereas, in 30.5% of patients, both anti-HBs and anti-HBc were positive.

Keywords: Immune response.Hepatitis B vaccination. Hemodialysis patients.Anti-HBs

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Introduction

Hepatitis B is a frequent global disease caused by hepatitis B virus.[1,2] Hepatitis B infects about two billion people worldwide, out of which chronic disease is present in 240 million individuals. Chronic disease causes cirrhosis and liver cancer. The annual mortality rate attributed to hepatitis B is 650,000 deaths per year across the globe.[3] Hepatitis B can manifest as asymptomatic, acute, fulminant, or chronic infection.[4]

Hemodialysis (HD) patients have greater chances of acquiring hepatitis B because of sharing of dialysis devices, need for repeated blood transfusions, and immunosuppression.[5,6] In hemodialysis patients, the frequency of hepatitis B varies according to the disease prevalence in that area and implementation of infection control practices.[4]

The hepatitis B virus (HBV) has 3 important antigens: hepatitis B core antigen (HBcAg), hepatitis B surface antigen (HBsAg) and hepatitis B e antigen (HBeAg). HBsAg is present in incubation period, acute infection and chronic infection. It is the most important test for the diagnosis of the infection. HBeAg appears in incubation period and acute disease. In chronic disease, HBeAg may be present or absent. Its presence shows rapid multiplication of the virus and a highly infective

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state. HBcAg is a component of viral nucleocapsid. Three types of antibodies are produced against hepatitis B. Hepatitis B surface antibody (anti-HBs) shows either the patient has been previously infected or vaccinated against hepatitis B.[4,7] If the patient has been previously infected with HBV, anti-HBc antibodies are also present in addition to anti-HBs.[8] The presence of anti-HBs only shows patient has been vaccinated with HBV vaccine. The cut-off value for protective anti-HBs levels is higher than 10 IU/L. Anti-HBs levels higher than 100 IU/L show effective protection. Hepatitis B core antibodies (anti-HBc) are of two types:[2,4] anti-HBc IgM in acute disease and anti-HBc IgG in chronic disease or after past infection.[7] Anti-HBc IgG once positive remain positive for life. Hepatitis B e antibody (anti-HBe) shows a low likelihood of transmission.[4]

Hepatitis B is diagnosed by specific serological tests. HBsAg and anti-HBc IgM are detectable in the serum in acute infection. The patients are labeled as having chronic hepatitis B if the HBsAg persists in the serum for more than six months. In the recovery phase, liver function tests (LFTs) become normal, HBsAg is negative and anti-HBs & anti-HBc IgG appear in the serum.[4]

Immunization is an important measure for the prevention of the disease. Hemodialysis patients have impaired immunity and vaccine does not produce protective anti-HBs levels in these patients. Anti-HBs titer also declines more rapidly with time in HD patients as compared to healthy individuals.[9,10] The vaccination schedule consists of 3 doses of 20µg vaccine given at 0,1 and 2 or 0,1 and 6 months. However, in HD patients, one additional dose of vaccine is given.[2] Anti-HBs levels should be monitored regularly in these patients and booster dose of vaccine administered in patients with low antibody titer.[10]

Hepatitis B is more prevalent in HD patients due to parenteral routes of the procedure in comparison to the general population. According to two studies conducted at hospitals in Lahore and Karachi, hepatitis B occurred in 10.6% and 10.2% of the hemodialysis patients, respectively.[11,12] This study was planned to evaluate the levels of isolated anti-HBs in HD patients. It will determine the percentage of patients who had developed adequate anti-HBs levels after vaccination. It will also guide us in scaling up of strict infection control practices in HD patients to prevent the disease transmission and assess the effect of hepatitis B vaccine on the anti-HBs levels.

Material and Methods

It was a cross-sectional descriptive study done at the Microbiology Department of Shaikh Zayed Hospital, Lahore after ethical approval (Ref No. F-39/ NHRC/ Admn/IRB/88). All the patients gave written consent for participation in the study.

Two hundred HBsAg negative patients were included by the convenient sampling technique. Their relevant history was documented on a Proforma sheet. Using the aseptic technique, blood sample was collected from each patient through venipuncture and centrifuged for 5 minutes at 5000 rpm to separate serum. Enzyme-linked immunosorbent assay (ELISA) was done to determine HBsAg in serum samples. Anti-HBs and anti-HBc antibody levels were detected in the serum samples of 200 HBsAg negative patients by using the ELISA kits. There was a minimum period of 6 weeks between the last vaccine dose and the collection of the blood samples. The anti-HBs titer more than 10 IU/L shows immunity and greater than 100 IU/L indicates very effective protection.

The data was analyzed with the Statistical Package for Social Sciences (SPSS) version 25. Mean & standard deviation (SD) were used for quantitative variables such as age. For qualitative variables such as gender and anti-HBs levels, frequency and percentages were used.

Results:

The average age of hemodialysis patients was 47.05+ 14.33 years, with the range of 12 years to 80 years,

Table 1: *Age, Gender and Vaccination Status of Hemodialysis Patients*

Age Groups (years)	Frequency	Percentage (%)
11-20	7	3.5
21-30	31	15.5
31-40	27	13.5
41-50	47	23.5
51-60	56	28.0
61-70	25	12.5
71-80	7	3.5
Gender	**Frequency**	**Percentage (%)**
Female	79	39.5
Male	121	60.5
Vaccination status	**Frequency**	**Percentage (%)**
Unvaccinated	7	3.5
Vaccinated	193	96.5

respectively. Out of 200 patients, there were 121(60.5%) males and 79(39.5%) females. In our study, 96.5% (193/200) of the patients had completed their vaccination course and only 3.5%(7/200) were unvaccinated (Table 1).

The mean period of hemodialysis was 48.21+42.21 months, ranging from 3 months to 264 months. Hypertension (HTN) was the etiological factor of renal disease in 42% of HD patients. The other causes were both diabetes and hypertension in 27% and diabetes mellitus in 6.5% of patients. The causes of renal disease are shown in figure 1.

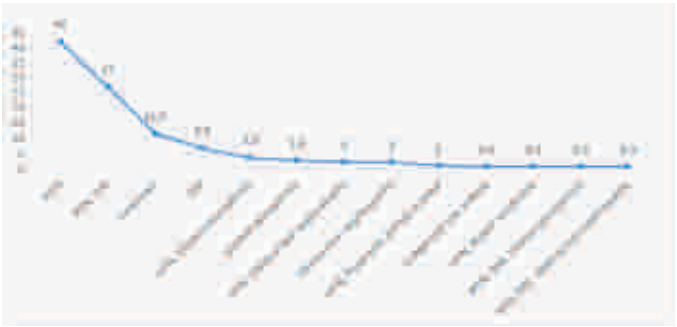

Figure 1: *Causes of End-Stage Renal Disease (in percentage)*

Out of 200 patients, 141(70.5%) patients were anti-HBs positive and 59(29.5%) patients were anti-HBs negative. Eighty (40%) patients were isolated anti-HBs positive whereas, in 61(30.5%) patients, anti-HBc was also positive in addition to anti-HBs. In 46(23%) patients, both anti-HBs and anti-HBc were negative. The serological markers of the patients are shown in figure 2.

Figure 2: *Serological Markers of the Study Subjects*

Among 193 patients who had received hepatitis B vaccination, anti-HBs was not detected in 55 patients. In 43(22.3%) patients, anti-HBc was also absent indicating that they had no previous infection. The vaccination response was poor in these patients. In 12(6.2%) patients, only anti-HBc was detected which indicated previous hepatitis B. Both anti-HBs and anti-HBc were detected in 60(31.1%) patients. Anti-HBs was produced in these patients after vaccination orpast infection. In total, there were 72 patients who with previous infection with positive anti-HBc. Vaccination is not required in these patients. In 78(40.4%) patients, anti-HBs was positive and anti-HBc was negative. These patients were responders as they developed protective antibody levels and there was no evidence of previous infection.

Out of 141(70.5%) anti-HBs positive patients, 62.5% patients had antibody titer between 10-100 IU/ml whereas only 8% patients had anti-HBs level >100 IU/L (Table 2).

Table 2: *Anti-HBs Titer in the Study Subjects*

Vaccination Status	Anti-HBs Levels			Total
	<10 IU/L	10-100IU/L	>100IU/L	
Vaccinated	55(27.5%)	122(61%)	16(8%)	193(96.5%)
Unvaccinated	4(2%)	3(1.5%)	0	**7(3.5%)**
Total	**59(29.5%)**	**141(70.5%)**	**0**	**200(100%)**

Discussion

Hepatitis B is a frequent infectious disease in patients undergoing hemodialysis. These patients are prone to acquire hepatitis B particularly if strict infection control measures are not undertaken.[10] The prevalence of disease varies in these patients worldwide.[13] As these patients have decreased immunity, majority of them do not develop anti-HBs after vaccination. In others, anti-HBs titer is low and it declines more rapidly with time.[14]

Our results showed that the hemodialysis patients had an average age of 47.05 years. There were 60.5% males and 39.5% females in our study. In a study by Ayub et al., the mean age of the hemodialysis patients was 55.1 years and 53% of them were females.[15] In another study by Mohammed et al., the mean age of hemodialysis patients was 48.5 years with 48% males & 52% females.[10]

In our study, the most common causes of kidney disease were hypertension and diabetes mellitus. Various studies have reported different etiological factors of renal disease. In a study in Karachi, Pakistan, the major cause of kidney disease was diabetes mellitus followed by renal stones and hypertension. Idiopathic disease was present in 40 patients.[11] In our study, 96.5% and 3.5% of the patients were vaccinated and unvaccinated, res-pectively. In a study by Guimaraes

et al, 73.8% of patients were vaccinated.[16]

In our study, 141(70.5%) patients were anti-HBs positive. with the antibody titer ranging from 10-100 IU/L in 62.5% of the patients and > 100 IU/L in 8% of the patients. In another study, the seroconversion rate was 100% in hemodialysis patients. All the patients were vaccinated. Sixty-four percent of the hemodialysis patients had anti-HBs levels ranging from 10-100 IU/L whereas, 36% of the patients had levels >100 IU/L.[10] The anti-HBs levels were lower in other studies. A study conducted in Brazil enrolled 83 hemodialysis patients. All the patients had received a complete course of vaccination. Out of these, 59% patients were anti-HBs positive whereas, 41% of patients were non-responders i.e. their anti-HBs levels were less than 10 IU/L. Most of the anti-HBs positive patients (37.3%) had a level > 100 IU/L whereas, 21.7% of the patients had levels between 10 to100 IU/L.[16] In another study done in Theran, 100 hemodialysis patients were included. All the patients were vaccinated with a four-dose vaccination regime. Anti-HBs was positive in 56.7% of patients.[17]

Conclusion

The anti-HBs levels were protective in 70.5% of the hemodialysis patients. The majority of the patients (62.5%) had antibody titer ranging between 10-100 IU/L and only 8% of the patients had antibody titer greater than 100 IU/L. Forty percent of patients were isolated anti-HBs positive whereas, in 30.5% of patients, both anti-HBs and anti-HBc were positive.

Recommendations

- We recommend that hemodialysis patients should be tested for anti-HBc and then vaccinated accordingly. Anti-HBc negative patients should be vaccinated according to the regime with monitoring of anti-HBs levels.
- In anti-HBc positive patients, HBsAg should be done. If HBsAg is positive, patients should be assessed for the disease stage and management. In HBsAg negative patients, vaccination is not required as these patients are already protected from previous infection.
- The anti-HBs levels produced after vaccination are low and fall with time in hemodialysis patients. Regular monitoring of anti-HBs levels should be done in these patients and booster doses administered if required.

References

1. Seto WK, Lo YR, Pawlotsky JM, Yuen MF. Chronic hepatitis B virus infection in hemodialysis patients. Lancet. 2018;392:2313-24.
2. Di Bisceglie AM, Lombardero M, Techman J, Roberts L, Janssen HLA, Belle SH, et al. Determination of hepatitis B phenotype using the biochemical and serological markers. J Viral Hepat. 2017 Apr;24:320-9. doi: 10.1111/jvh.12643.
3. Zhang L, Gui XE, Wang B, Fan JY, Cao Q, Mullane K, et al. Serological positive markers of hepatitis B virus in femoral venous blood or umbilical cord blood should not be evidence of in-utero infection among neonates. BMC InfectDis. 2016;16:408. doi: 10.1186/s12879-016-1754-1.
4. Song JE, Kin DY. Diagnosis of hepatitis B. Ann Transl Med. 2016 Sep;4:338.doi: 10.21037/atm. 2016. 09. 11.
5. Al Zabadi H, Rahal H, FuqahaR. Hepatitis B and C prevalence among hemodialysis patients in the West Bank hospitals, Palestine. BMC Infect Dis.2016; 16:41. doi: 10.1186/s12879-016-1359-8.
6. Soi V, Soman S. Preventing hepatitis B in the dialysis unit. Adv Chronic Kidney Dis. 2019 May;26:179-84. doi: 10.1053/j.ackd.2019.03.003.
7. Easterbrook PJ, Roberts T, Sands A. Peeling R. Diagnosis of viral hepatitis. CurrOpin HIV AIDS. 2017 May; 12:302-14. doi: 10.1097/ COH. 0000000000000370.
8. Yuen MF, Chen DS, Dusheiko GM, Janssen HLA, Lau DTY, Locarnini SA. Hepatitis B virus infection. Nat Rev Dis Primers. 2018 Jul;18035. doi: 10.1038/ nrdp. 2018. 35.
9. Trepo C, Chan HLY, Lok A. Hepatitis B virus infection. Lancet. 2014;384:2053-63.
10. Mohammad HI, El-Hefenawy SM, Mohamed SF. Assessment of immune response to hepatitis B virus vaccine in chronic hemodialysis patients. Menoufia Med J. 2017;30:184-9.
11. Anwar K, Imran M, Shahzad F, Noreen M, Atif M, Ahmad F, et al. Prevalence of hepatitis B and hepatitis C among patients undergoing dialysis. J Hum Virol Retrovirol. 2016;33:00094.doi: 10.15406/ jhvrv. 2016. 03.00094.
12. Alkhan AA. Hepatitis B virus (HBV) and hepatitis C virus (HCV) infections among hemodialysis patients. General Med. 2015; 3:1. doi: 10.4172/2327-5146. 1000165.
13. Tajbakhsh R. Prevalence of hepatitis C and B virus infections among hemodialysis patients in Karaj, Iran. Saudi J Kidney Dis Transpl. 2015 Jul-Aug;26:792-6. doi: 10.4103/1319-2442.160219.

14. Ong KY, Wong HY, Khee GY. What is the hepatitis B vaccination regime in chronic kidney disease? Cleve Clin J Med. 2018Jan;85:32-4.doi: 10.3949/ ccjm. 85a. 17017.
15. Ayub MA, Bacci MR, Fonseca FLA, Chehter EZ. Hemodialysis and hepatitis B vaccination: a challenge to physicians. Int J Gen Med. 2014;7:109-14. doi: 10. 2147/1jgm.S57254.
16. Guimaraes MNC, Facincani T, Santos SSD.Hepatitis B status in hemodialysis patients. Arq Gastroenterol. 2017 Dec; 54: 356-8. doi: 10. 1590/ s0004-2803. 201700000-34.2017.
17. Ramezani A, Aghasadeghi MR, Ahmadi F, Razeghi E, Eslamifar A, Banifazl M, et al. Isolated anti-HBc and occult HBV infection in dialysis patients. Nephrourol Mon. 2015 Jan;7:e22674. doi: 10.5812/ numonthly. 22674.

Authors Contribution

AA: Conceptualization of Project
MI: Data Collection
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SQ: Statistical Analysis
KNS: Drafting, Revision
MA: Writing of Manuscript

Questionnaire Survey of Urologists Concerning Chronic Prostatitis and Chronic Pelvic Pain Syndrome

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Abstract

Objective: To perform a questionnaire survey among urologists to determine issues about presentation, work-up and management of Chronic Prostatitis and CPPS.

Method: It was a Questionnaire Survey, which was done in Department of Urology, SIMS/Services Hospital Lahore during the period March 2019 to September 2019. Non-probability Convenient sampling technique was used. A detailed questionnaire regarding workup and management of CP/CPPS was circulated by e-mail among 100 Consultant urologists, all over Pakistan with more than 3 years post fellowship clinical experience in tertiary care hospitals. These urologists were requested to fill the questionnaire forms then data was analysed on IPSS 20 and resulted were generated.

Results: Most of the urologists responded that patients have multiple symptoms. Most common were lower urinary tract symptoms (92%) and perennial pain (55%). None of the urologists were accustomed to applying (NIH) chronic prostatitis symptoms score. About 45% perform digital rectal examination. Four glass test is practiced by only 4% of our urologists, while most perform urine microscopy and culture (82%). About half of the urologists get abdominal ultrasound done before initiating treatment. Although many urologists (43%) think that this diagnosis of exclusion is not infective in nature but still choose broad spectrum antibiotics as first line. Quinolones are preferred by majority (84%) of urologists. For symptomatic relief, alpha-blockers are prescribed by 62% urologists and NSAIDS by 72%, whereas spasmolytics are used less frequently (28%). Therapeutic prostatic massage is being practiced by 15% of the urologists and they feel that it is useful. Transurethral resection of prostate in not recommended by any urologist.

Conclusion: There is no appropriate following of standard protocols in our urology community and a hit and run attitude is followed. We need proper randomized controlled trials in our population and formulation of national guidelines on this issue.

Keywords: diagnosis of exclusion, chronic prostatitis, CPPS

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Introduction

Prostatitis is the most common urologic diagnosis in men younger than 50 years and the third most common urologic diagnosis in men older than 50 years after benign prostatic hyperplasia (BPH) and prostate cancer. In spite of recent advances in urology chronic prostatitis/CPPS remains a poorly understood condition. It is a debilitating disease and has detrimental effects on patients 'quality of life (QOL). It affects men of wide age range. Condition is not uncommon, prevalence range

in USA is 2 to 10% in general population.[1]

The cause is unknown. Diagnosis involves ruling out other potential causes of the symptoms such as bacterial prostatitis, benign prostatic hypertrophy, overactive bladder, and cancer.[2]

Chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS) is characterized by pelvic or perineal pain without evidence of urinary tract infection, lasting longer than 3 months, as the key symptom.[3] Symptoms may wax and wane. Pain can range from mild to debilitating. Pain may radiate to the back and rectum, making sitting uncomfortable. Pain can be present in the perineum, testicles, tip of penis, pubic or bladder area. Dysuria, arthralgia, myalgia, unexplained fatigue, abdominal pain, constant burning pain in the penis, and frequency may all be present. Frequent urination and increased urgency. Post-ejaculatory pain, mediated by nerves and muscles, is a hallmark of the condition and serves to distinguish CP/CPPS patients from men with BPH or normal men. Some patients report low libido, sexual dysfunction and erectile difficulties.[4]

The terminology has changed rapidly over the past half a century. Various terms like prostatitis, prostatitis syndrome, prostate-dynia and chronic pelvic pain syndrome (CPPS) have been used at different times. This proves poor understanding of this conditions. National Institute of Health (NIH) symptoms index was devised in 1995 to quantify the symptoms. Although NIH classification has increased understanding of the disease but it has its limitations.[5]

There are no definitive diagnostic tests for CP/CPPS. It is a poorly understood disorder, even though it accounts for 90–95% of prostatitis diagnoses. CP/CPPS may be inflammatory (Category Ⅲa) or non-inflammatory (Category Ⅲb), based on levels of pus cells in expressed prostatic secretions (EPS), but these subcategories are of limited use clinically. In the inflammatory form, urine, semen, and other fluids from the prostate contain pus cells (dead white blood cells or WBCs), whereas in the non-inflammatory form no pus cells are present. Recent studies have questioned the distinction between categories Ⅲa and Ⅲb, since both categories show evidence of inflammation if pus cells are ignored and other more subtle signs of inflammation, like cytokines, are measured.[6]

Recommended treatments include multimodal therapy including physiotherapy, alpha blocker medication, antibiotics and anti-inflammatory drugs in certain newly diagnosed cases.[7] Tentative evidence supports some non-medication based treatments.[8]

Literally prostatitis means inflammation of the gland but many patients may not have any signs of inflammation. It even includes clinical situations in which prostate is apparently not involved. That is why term CPPS was introduced for these patients.[3]

Disease usually runs a chronic course leading to frustration and anger among the sufferers. Treating doctors are also at times frustrated because of lack of response. [9]

No universally accepted guidelines are available for evaluation and treatment. Many urologists have devised their own protocol of work up and management.[10]

This study was carried out in order to find out how the local urologists are dealing with CP/CPPS in our country.

Material and Methods

It was a Questionnaire Survey, which was done in Department of Urology, SIMS/Services Hospital Lahore during the period March 2019 to September 2019. Non-probability Convenient sampling technique was used. A detailed questionnaire regarding workup and management of CP/CPPS was circulated by e-mail among 100 Consultant urologists, all over Pakistan with more than 3 years post fellowship clinical experience in tertiary care hospitals. These urologists were requested to fill the questionnaire forms then data was analysed on IPSS 20 and resulted were generated.

Results

The most common age group that is reported by urologists is 40-50 years (42%). Almost all the urologists examine 1-5 patients of CP/CPPS every month. Symptoms vary widely but the most common symptoms reported are lower urinary tract symptoms (92%) and perennial pain (55%). None of the urologists use NIH chronic prostatitis symptoms index. In this survey, only 45% perform digital rectal examination.

Only 4% of urologists believe in 4-glass test, while most carried out urine microscopy and culture (82%) to differentiate chronic bacterial prostatitis from a-bacterial category. About half of the urologists get abdominal ultrasound done. Only a small percentage (10%) of urologists believe in estimation of Serum Prostatic Specific Antigen (P.S.A). Transrectal ultrasound, urodynamics and cystoscopy are not routinely advised by any urologist.

Although many urologists (43%) thought CPPS as diagnosis of non-infective origin, still they choose antibiotics as front line weapons. Quinolones are preferred by majority (84%). Alpha-blockers are prescribed by 62% urologists and NSAIDS by 72%, whereas spasmolytics are being used by 28% of the urologists. The most common secondary therapies include anti-depressants (86%), pregabalins (65%), skeletal muscle relaxants (15%), phytotherapy (20%) and hormonal treatment (5%). Therapeutic prostatic massage is being practiced by 15% of the urologists and they feel that it is useful. Transurethral resection of prostate in not recommended by any urologist. 67% percent urologists are dissatisfied with the current management of chronic prostatitis/ CPPS and feel pessimistic about it.

Discussion

Classification of chronic prostatitis/CPPS has been changing rapidly. Drach et al (1978) classification was widely accepted for a long time but later NIH classification introduced in 1999 has gradually replaced Drach classification. In the new classification category III replaced old terms of chronic abacterial prostatitis and prostatodynia.[11]

Clinical examination is usually unremarkable in these patients. There was no consensus on digital rectal examination, in this survey with less than half of the urologists performing DRE while others think it is useless.[12] In a similar survey conducted in Korea showed about 81% urologists perform DRE in their patients.[13] Mainstay of diagnostic evaluation has been 4 glass test introduced by Mears and stamey in 1968. Many urologists all over the world have given up this test because of its complexity. According to this survey, only 4% urologists perform 4 glass test in our set up. A shortcut in the form 2 glass test has been advocated which involves pre and post massage samples.[14]

Other diagnostic tools include urine and semen C/S. In this study majority (82%) of the urologists used urine culture for the diagnosis rather than 4-glass or 2-glass test. They believe that 4-glass test is cumbersome and time consuming. According to a Chinese survey conducted in 2008 only 20% number of their urologists believed in urine cultures.[15]

Serum PSA is an optional investigation and not frequently done in our setup. Only 10% of urologists advise PSA in this study[16]. It may be raised in acute or in chronic prostatitis. Values upto 20ug/nl have been reported. PSA levels may take 6 weeks or longer to settle down. 17 According to this survey, optional tests as uroflow, urodynamics, urethography, urine cytology, cystoscopy and CT were not routinely used.[18]

Etiology of C.P.P.S is not clearly understood in most of the patients. There are conflicting views about infectious etiology of the disease. Definitive diagnosis of chronic bacterial prostatitis requires presence of organisms in urine or prostatic fluid. Urine cultures are positive in less than 10% of patients.[19] About 43% of our urologists believe that etiology is not infectious. In spite of this concept most of the urologists use antibiotics as first line treatment because many patients respond[13]. Results of similar surveys involving Japanese, Chinese and Korean urologists are comparable with our study.[3,13]

As far as Management of chronic prostatitis/CPPS is concerned all the urologists who took part in the survey use antibiotics as primary treatment. Even if urine culture is negative, most of the urologists prefer to use antimicrobial agents as primary treatment.[20]

In spite of emerging resistance with fluroquinolones, they are still preferred by 84% of our urologists. Ciprofloxacin is still the most commonly used antimicrobial[7]. Tetracycline and trimethoprime are used less frequently. According to Japanese survey antibiotics were used less frequently, preferred by 61.9% of their urologists[21]. In their study fluroquinolones and trimethoprim were the most frequently used antibiotics. Carnitine pollen solution was the second most popular treatment used by 55.5% where Pollen extract is rarely used in our setup. Antibiotics are also the first choice of the urologist in other studies as well.[22]

A large percentage of our urologists believe that anti-inflammatory drugs are useful in the management. They are usually prescribed in combination with antibiotics.[8] Anti-inflammatory drugs are not used as frequently use by the other urologists as reported in their surveys. In this survey most common secondary therapies are anti-depressant and pregabalins. Pregabalins have been recently launched and their efficacy has not been established so far.[23] According to some studies some urologists refer these patients for Psychotherapy, however it is not recommended in our setup.[24]

This survey reveals that there is no definite protocol for evaluation and management of chronic prostatitis/ CPSS. Different urologists evaluate and treat this condition according to their own experience.

Conclusion

There is no appropriate following of standard protocols in our urology community and a hit and run attitude is followed. We need proper randomized controlled trials in our population and formulation of national guidelines on this issue.

Conflict of Interest : None

References:

1. Schaeffer AJ, Landis JR, Knauss JS, et al. Chronic prostatitis collaborative research network group. Demographic and clinical characteristics of men with chronic prostatitis: the national institute of health chronic prostatitis cohort study. J Urol 2002;168(2):593-8.
2. Weidner W, Schiefer HG, Krauss H, et al. Chronic prostatitis: a thorough search for etiologically involved microorganisms in 1461 patients. Infection 1991; 19: 119-25.
3. Nickel JG, Wagenlehner F, Pontari M, et al. Male chronic pelvic pain syndrome (CPPS). In: Chapple G, Abrams P, editors. Male lower urinary tract symptoms (LUTS). An international consultation on male LUTS, Fukuoka, Japan, Sept 30-Oct 4, 2012. Montral: Societe Internationale d'Urology (SIU); 2013. P. 331-72.
4. Wagenlehner FME, VanTill JW, Magri V, et al. National institutes of health chronic prostatitis symptom index (NIH-CPSI) symptom evaluation in multinational cohorts of patients with chronic prostatitis/chronic pelvic pain syndrome. Eur Urol 2013;63(5):953-9.
5. Kavoussi PK, Costabile Ra. Orchialgia and the chronic pelvic pain syndrome. World J Urol 2012;31:773-8.
6. Holt JD, Garrett WA, McCurry TK, Teichman JM (2016). "Common Questions About Chronic Prostatitis". Am Fam Physician. 93 (4): 290–6. PMID 26926816.
7. Duclos, AJ.; Lee, CT.; Shoskes, DA. (Aug 2007). "Current treatment options in the management of chronic prostatitis". Ther Clin Risk Manag. 3 (4): 507–12. PMC 2374945. PMID 18472971
8. Franco, JV; Turk, T; Jung, JH; Xiao, YT; Iakhno, S; Garrote, V; Vietto, V (12 May 2018). "Non-pharmacological interventions for treating chronic prostatitis/chronic pelvic pain syndrome". The Cochrane Database of Systematic Reviews. 5: CD012551. doi:10.1002/14651858.CD012551.pub3. PMC 6494451. PMID 29757454.
9. Jump up to:a b c Doiron, RC; Nickel, JC (June 2018). "Management of chronic prostatitis/chronic pelvic pain syndrome". Canadian Urological Association Journal. 12 (6 Suppl 3): S161–S163. doi: 10. 5489/ cuaj. 5325. PMC 6040620. PMID 29875042.
10. Anothaisintawee T, Attia J, nickel JC, et al. The management of chronic prostatitis/chronic pelvic pain syndrome: a systematic review and network meta-analysis. JAMA 2011;305:78-86.
11. DRACH GW, Fair WR, Meares EM, et al. Classification of benign disease associated with prostatic pain: prostatitis or prostatodynia? J Urol 1978; 120 (2):266.
12. Litwin MS, McNaughton Collins M, Fowler FJ Jr, et al. The national institutes of health chronic prostatitis symptom index: development and validation of a new outcome measure. J Urol 1999;162(2):369-75.
13. Nickel JC, Shoskes D. Phenotypic approach to the management of chronic prostatitis/chronic pelvic pain syndrome. Curr Urol Rep 2009;10(4):307-12.
14. Jump up to:a b Doiron, RC; Nickel, JC (June 2018). "Evaluation of the male with chronic prostatitis/ chronic pelvic pain syndrome". Canadian Urological Association Journal. 12 (6 Suppl 3): S152–S154. doi: 10.5489/cuaj.5322. PMC 6040610. PMID 29875039.
15. Nickel JC, Alexander RB, Schaeffer AJ, et al. Leukocytes and bacteria in men asymptomatic controls. J Urol 2003;170(3):818-22.
16. Tracy Cr, Steers WD, Costabile R. Diagnosis and management of epididymitis. Urol Clin North Am 2008; 35(1):101-8.
17. Pontari MA, Ruggieri Mr. Mechanisms in prostatitis/chronic pelvic pain syndrome. J Urol 2004; 172(3): 839-45.
18. Schaeffer Aj. Chronic prostatitis and chronic pelvic pain syndrome. N Engl J Med 2006;355:1690-8.
19. Schaeffer AJ (2007). "Epidemiology and evaluation of chronic pelvic pain syndrome in men". Int J Antimicrob Agents. 31: S108–11. doi:10.1016/ j.ijantimicag. 2007.08.027. PMID 18164597.
20. Nickel JC, Shoskes DA, Wagenlehner FM. Management of chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS): the studies, the evidence and the impact. World J Urol 2013;31:747-53.
21. Clemens, J Quentin; Meenan, Richard T; O'Keeffe Rosetti, Maureen C; Gao, Sara Y; Calhoun, Elizabeth A (Dec 2005). "Incidence and clinical characteristics of National Institutes of Health type III prostatitis in the community". J Urol. 174 (6): 2319–22. doi: 10. 1097/01.ju.0000182152.28519.e7. PMID 16280832.
22. Luzzi GA (2002). "Chronic prostatitis and chronic pelvic pain in men: aetiology, diagnosis and management". Journal of the European Academy of Dermatology and Venereology. 16(3): 253–6. doi:10.1046/j.1468-3083. 2002.00481.x. PMID 12195565.

23. Franco, JVA (14 May 2018). "Intervention for treating chronic prostatitis and chronic pelvic pain in men". The Cochrane Database of Systematic Reviews. 5: CD012551. doi:10.1002/ 14651858.CD012551. pub3. PMC 6494451. PMID 29757454. Retrieved 11 March 2019.
24. Nickel, JC.; Tripp, DA.; Chuai, S.; Litwin, MS.; McNaughton-Collins, M.; Landis, JR.; Alexander, RB.; Schaeffer, AJ.; et al. (Jan 2008). "Psychosocial variables affect the quality of life of men diagnosed with chronic prostatitis/chronic pelvic pain syndrome". BJU Int. 101(1): 59–64. doi:10.1111/j.1464-410X. 2007. 07196. x. PMID 17924985.

Authors Contribution

AM: Conceptualization of Project
AAS: Data Collection
NS : Literature Search
AA: Statistical Analysis
ZAR: Drafting, Revision
MSA: Writing of Manuscript

Gender Difference on Sleep Quality Among Medical Students

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Abstract

Objective: This cross-sectional study was designed to determine prevalence of sleep quality among medical students and to find out if there is any difference in quality of sleep among male and female medical students.

Method: In this cross-sectional study, total of 221 first year medical students from Bachelor of Medicine and Bachelor of Surgery (MBBS) and Bachelor of Dental Sciences (BDS) were included by non-probability convenient sampling technique. The semi structured questionnaire included a 12 item demographics section and the PSQI, SDQ questionnaire to assess sleep quality and sleep disorders. Data analysis was done using SPSS 25.0. Chi-square test was used and P value <0.05 was taken as significant.

Results: A greater percentage of females as compared to males were "Poor sleepers" (91.4% females as compared to 84% males). The consumption of coffee/tea/caffeinated drinks per day was associated with gender (0.040). Although there was found no association between the global PSQI score and gender (0.470) but females experienced greater difficulties than males to go to sleep within 30 minutes (.038)

Conclusion: This is the first study that aims to find out association between gender and sleep quality in first year medical students. Whilst, study did not report any statistically significant difference of sleep quality with gender, but there was an alarmingly high prevalence rate of very poor sleep quality among medical students and females were suffering more from poor quality of sleep as compare to male students. Students should be counselled on the topic of sleep health and taught to abstain from self-medication with caffeine.

Keywords: Sleep quality, PSQI, Medical students

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Introduction

Sleep quality is defined as one's satisfaction of the sleep experience, integrating aspects of sleep initiation, sleep maintenance, sleep quantity, and refreshment upon awakening. Whilst, it has been reported that a good quality of sleep is essential to the memory process,[1] almost half of university students experience poor sleep quality.[2] This incidence can be attributed to technology, particularly the use of it at bedtime, which has been proven to decrease sleep quality[3], as well as the consumption of tobacco and an unhealthy lifestyle.[4] But perhaps the most predominant factor and one particularly applicable to medical students is "Academic Stress". Considerably higher levels of stress and associated poor sleep quality have been reported in medical students as compared to other professional students,[5] so much so that 77% of Pakistani medical students have reported poor sleep quality.[6]

According to the Pakistan medical system, an MBBS degree consists of two preclinical years and three clinical years. Whilst first year medical students have just made the life changing experience of just entering medicine, they haven't been the subject of many researches;

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Mojtaba et al[7] concluded that no extensive study on the sleep condition of medical students at pre-clinical stages has been carried out, but they fail to make any comparison between the individual preclinical medical years. Another research conducted in Botucatu, Brazil reported first and second year medical students having greater daytime dysfunction and sleep quality worse than medical students in other years of study.[8] Amina Nadeem et al results suggested that the mean nocturnal sleep period was significantly shorter for 1st year medical students than for 2nd year medical students.[9] Another study was conducted by Jaydeep et al in which 83% of students reported that they had experienced a change in sleeping pattern after getting admission in M.B.B.S.[10]

There has been a widely reported disparity in sleep quality between the two genders. Males on average tend to have better sleep quality,[11] sleep quality significantly associated with lifestyle factors[11] and smartphone addiction,[12] and higher mortality when associated with difficulties initiating sleep[13] in comparison to women. Females on the other hand, have a higher incidence of myocardial infarction when sleep deprived and difficulties maintaining sleep and an overall prevalence of poor sleep quality as compared to their male counterparts.[14] It has already been established that medical students experience greater stress and hence worse sleep quality than students of other studies.[15]

Keeping in view all the above factors, this study was designed to determine prevalence of sleep quality among 1st year medical students and to find out if there is any difference or association in quality of sleep between male and female medical students.

Material and Methods

The setting of this cross-sectional study was (here text hide from Editor) and comprised of 221 newly enrolled healthy 1st year medical students of both MBBS and BDS. It was approved by the Ethical Review Committee.

The sample size was calculated to be 221 students using the following formula $n = Z^2 1 - \alpha/2\ p(1-p) / d^2$ with 95% confidence interval and 5% error margin.

After taking informed written consent, all healthy 1st year medical students inclusive of the age group 17-23 were included in the study by non-probability convenient sampling technique. Students diagnosed with a sleep disorder (apnea, insomnia), or students medicating themselves already for a sleep disorder were excluded from the study.

Pre-tested and semi structured questionnaires designed in English language were distributed to the students in a classroom setting. The first section consisted of 12 questions pertaining to the demographics of the subject. The latter portion of this designed questionnaire included the Pittsburgh sleep quality index (PSQI)[16] and sleep disorders questionnaire (SDQ).[12] The PSQI pertains to the various aspects of the sleep quality, habits and hygiene of the subject. It derives 7 components of sleep; subjective sleep quality, sleep latency, sleep quality, sleep efficiency, sleep disturbance, sleep medication, and daytime dysfunction by scaling it on an equally reflective scale for all the components of 0 to 3 from none too severe. The Global PSQI Score is obtained by simply summing the scores of the all the 7 components. A global sum of "5"or greater indicates a "poor" sleeper, whereas those with a global sum of less than "5" are labeled as "good" sleepers. The PSQI questionnaire has a diagnostic specificity of 86.5% and a sensitivity of 89.5%.[16] The data was analyzed using SPSS 25.0. Qualitative variables were presented in the form of frequencies and percentages. Chi-square test was used to determine association between two groups. P-value <0.05 was taken in consideration to be significant.

Table 1: *Basic characteristics of study participants*

Characteristic	Participants (n=384) No. (%)
Sex	
Male	81 (36.7%)
Female	140 (63.3%)
Age (years)	
18	55 (24.9%)
19	110 (49.8%)
20	51 (23.1%)
21	5 (2.3%)
Discipline	
MBBS	146 (66.1%)
BDS	75 (33.9%)
Social Background	
Rural	11 (5%)
Semi-Urban	36 (16.3%)
Urban	174 (78.7%)
Hostelite/Day Scholar/Medical Cadet	
Hostelite	96(43.4%)
Day Scholar	95 (43.0%)
Medical Cadet	30 (13.6%)

Results

Out of 221 participants, there were 146 students from MBBS (66.1%), and 75 students from BDS (33.9%). There were 140 female students (63.3%) and 81 male students (36.7%). Table 1

Overall a greater percentage of females as compared to males were "Poor sleepers" (91.4% females as compared to 84% males). Overall, total 89.6% students reported that they took less than 7 hours sleep. There were 29.1% females who only take less than 5 hours sleep and 16% males also reported the same finding

In sleep disorder questionnaire, there were four questions in which we found significantly higher number of females suffering from symptoms of sleep disorders as compare to male, significant p-value, Do you have trouble falling asleep? (0.006). Do you take anything to help you sleep? (0.073) Do you feel sad, irritable or hopeless? (0.000) Do you feel nervous or worried? (0.000). Also females reported a higher PSQI score; the highest global PSQI score reported by a male was 13, whereas the highest global PSQI score reported by a female was 16. Also, the number of females who had a PSQI score of 10 and above were 36; the number

Table 2: *Frequency distribution of sleep quality measured by PSQI*

Sleep disturbances(during past month)	Gender	Not During the Past month (0)	Less than once a week (1)	Once or twice a week (2)	Three or more times a week (3)	P-value
a. Cannot go to sleep within 30 minutes	**Female**	31.4%	21.4%	18.6%	28.6%	.038*
	Male	38.3%	22.2%	27.2%	12.3%	
b. Wake up In the middle of the night or early morning	**Female**	35.7%	25.7%	22.1%	15.7%	.076
	Male	49.4%	29.6%	14.8%	6.2%	
c. Have to get up to use the bathroom	**Female**	53.6%	25.7%	14.3%	6.4%	.483
	Male	50.6%	34.6%	9.9%	4.9%	
d. Cannot breathe comfortably	**Female**	80.7%	8.6%	8.6%	2.1%	.112
	Male	91.4%	6.2%	1.2%	1.2%	
e. Cough or snore badly	**Female**	91.4%	5.0%	2.9%	0.7%	.562
	Male	86.4%	6.2%	4.9%	2.5%	
f. Feel too cold	**Female**	51.4%	22.1%	18.6%	7.9%	.017*
	Male	64.2%	27.2%	6.2%	2.5%	
g. Feel too hot	**Female**	55.0%	27.9%	12.1%	5.0%	.483
	Male	48.1%	27.2%	19.8%	4.9%	
h. Have bad dreams	**Female**	41.4%	30.0%	18.6%	10.0%	.217
	Male	50.6%	32.1%	13.6%	3.7%	
i. Have pain	**Female**	60.7%	24.3%	10.0%	5.0%	.165
	Male	72.8%	18.5%	3.7%	3.7%	
How often have you taken medicine (prescribed as "over the counter" to help you sleep?	**Female**	88.6%	2.1%	3.6%	5.7%	.169
	Male	90.1%	6.2%	2.5%	1.2%	
How often have you had trouble staying awake while driving, eating meals, or engaging in social activities?	**Female**	17.1%	17.9%	26.4%	38.6%	.826
	Male	21.0%	19.8%	25.9%	33.3%	
How much of a problem has it been for you to keep enthusiasm to get things done?	**Female**	12.9%	35.7%	32.1%	19.3%	.635
	Male	18.5%	35.8%	30.9%	14.8%	
		Very good (0)	**Fairly Good (1)**	**Fairly Bad**	**Very Bad (3)**	
Rate your sleep quality overall	**Female**	12.1%	49.3%	32.1%	6.4%	.323
	Male	21.0%	48.1%	25.9%	4.9%	

of males on the other hand was 14. However, there was found to be no association between the global PSQI score and gender (p value = 0.470). The consumption of coffee/tea/caffeinated drinks per day was greater in the female population than the male population and was positively associated with gender (p value = 0.040). Also females experienced greater difficulties than males to go to sleep within 30 minutes, (p value 0.038). No association was observed between obstructive sleep symptoms and gender (cannot breathe comfortably (0.112) and cough or snore badly (0.562). 6.4% females and 4.9% males rated their overall sleep quality very bad.(.323) Table 2.

Discussion

Our findings suggest that first year medical students have very poor sleep quality and this finding was supported by previous studies.[17-20] This study found out that 89.6% participants take less than 7 hours sleep. The prevalence of poor sleep quality in this study is higher than reported in literature, with the prevalence of poor sleep quality ranging between 30% and 59%.[21] Although a greater percentage of females are 'poor sleepers', but there is no statistical difference between male and female sleep quality in this study.

Results of this study showed a very high prevalence of poor sleep quality among medical students, with males tending to be only slightly better than their female counterparts; not only this but females also found it more difficult to go to sleep (28.6%) three and more times a week, 5.7% females had to take something to help them sleep while only 1.2% males suffered from this problem. Results of the study done by Surani et al supported these findings.[22] This was also supported by two more studies who stated in their study that as compared to the 20% of males, 66% of females suffer from severe problem and psychological distress.[23-24]

In our study, the consumption of coffee/tea/ caffeinated/ energy drinks per day was greater in the female population than the male population and was positively associated with gender (p-value = 0.040). The poor sleep quality of women as compared to men can be suggested to be to the increased caffeine intake of women as compared to men. This is in line with a study where participants who consumed energy drinks had PSQI scores higher than those participants who did not.[24] However, there are other studies that disagree with this notion, stating that caffeine consumption does not predict difficulties inducing sleep or other sleep disturbances.[25]

Conclusion

This study did not find any association of sleep quality with gender among medical students but there was an alarmingly high prevalence rate of very poor sleep quality among medical students and females were suffering more from poor quality of sleep as compare to male students. Medical students are already an increased risk for various mental disorders owing to the tremendous stress placed on them. To see students having this poor sleep quality at such an early stage of their medical study surely prompts the need for immediate action. Students should be counselled on the topic of sleep health and taught to abstain from self-medication with caffeine.

Limitation

Sample size of 221 students is not sufficient to generalize our findings for all Pakistani medical students; thus it should be done on greater sample size and include other medical colleges. Also, to produce more concrete results, these first year students should be followed up in the next year too to determine the presence of factors unique to first year that could account for their sleep quality.

References

1. Vyazovskiy VV. Sleep, recovery, and metaregulation: explaining the benefits of sleep. Nat Sci Sleep. 2015; 7: 171-184. doi: 10.2147/NSS.S54036
2. Oginska H, Pokorski J. Fatigue and mood correlates of sleep length in three age-social goups: school children, students, and employees. Chronobiol Int. 2006; 23 (6): 1317–1328. DOI:10.1080/07420520601089349
3. Fuller C, Lehman E, Hicks S, Novick MB. Bedtime Use of Technology and Associated Sleep Problems in Children. Glob Pediatr Health. 2017; 4: 2333794X 17736972.Doi: 10.1177/2333794X17736972
4. Araújo MF, Freitas RW, Lima AC, Pereira DC, Zanetti ML, Damasceno MM. [Health indicators associated with poor sleep quality among university students]. Rev Esc Enferm USP. 2014; 48(6):1085-92. doi: 10.1590/ S0080-623420140000700017.
5. Jafri SAM, Zaidi E, Aamir IS, Aziz HW, Imad-ud-Din, Shah MAH, et al. Stress Level Comparison of Medical and Non-medical Students: A Cross Sectional Study done at Various Professional Colleges in Karachi, Pakistan. Acta Psychopathol. 2017, 3:2. doi: 10.4172/ 2469-6676.100080

6. Waqas A, Khan S, Sharif W, Khalid U, Ali A. Association of academic stress with sleeping difficulties in medical students of a Pakistani medical school: a cross sectional survey. PeerJ. 2015;3:e840. Published 2015 Mar 12. doi:10.7717/peerj.840.
7. Rezaei M, Khormali M, Akbarpour S, Sadeghniiat-Hagighi K, Shamsipour M. Sleep quality and its association with psychological distress and sleep hygiene: a cross-sectional study among pre-clinical medical students. Sleep Sci. 2018;11(4):274-280. doi: 10.5935/1984-0063.20180043
8. Corrêa CC, Oliveira FK, Pizzamiglio DS, Ortolan EVP, Weber SAT. Sleep quality in medical students: a comparison across the various phases of the medical course. J Bras Pneumol. 2017;43(4):285-289. doi: 10.1590/S1806-37562016000000178
9. Nadeem DA, Cheema M, Naseer M, Javed H. ASSESSMENT OF SLEEP QUALITY AND PATTERNS SUGGESTIVE OF SOMNIOPATHIES AMONG STUDENTS OF ARMY MEDICAL COLLEGE, RAWALPINDI. PAFMJ [Internet]. 28Feb.2018 [cited 9May2020];68(1):143-8.
10. Devaliya JJ, Chawada BL. A Cross-Sectional Study of Change in Sleep Pattern among First year Students of a Medical College in Western India. Indian Journal of Forensic and Community Medicine, October-December 2017;4(4):270-273. DOI: 10.18231/2394-6776.2017.0059
11. Fatima Y, Doi SA, Najman JM, Mamun AA. Exploring Gender Difference in Sleep Quality of Young Adults: Findings from a Large Population Study. Clin Med Res. 2016;14(3-4):138-144. doi:10.3121/ cmr. 2016. 1338
12. Kumar VA, Chandrasekaran V, Brahadeeswari H. Prevalence of smartphone addiction and its effects on sleep quality: A cross-sectional study among medical students. Ind Psychiatry J. 2019;28(1):82-85.doi: 10.4103/ ipj.ipj_56_19
13. Lallukka T, Podlipskytė A, Sivertsen B, et al. Insomnia symptoms and mortality: a register-linked study among women and men from Finland, Norway and Lithuania. J Sleep Res. 2016;25(1):96-103. doi: 10.1111/jsr. 12343
14. Azad MC, Fraser K, Rumana N, et al. Sleep disturbances among medical students: a global perspective. J Clin Sleep Med. 2015;11(1):69-74. Published 2015 Jan 15. doi:10.5664/jcsm.4370
15. Mishra J, Panigrahi A, Samanta P, Dash K, Mahapatra P, Behera MR. Sleep quality and associated factors among undergraduate medical students during Covid-19 confinement. Clinical Epidemiology and Global Health. 2022 May 1;15:101004. https:// doi. org/ 10.1016/j.cegh.2022.101004
16. Mollayeva T, Thurairajah P, Burton K, Mollayeva S, Shapiro CM, Colantonio A. The Pittsburgh sleep quality index as a screening tool for sleep dysfunction in clinical and non-clinical samples: A systematic review and meta-analysis. Sleep medicine reviews. 2016 Feb 1;25:52-73.
17. Surani AA, Zahid S, Surani A, Ali S, Mubeen M, Khan RH. Sleep quality among medical students of Karachi, Pakistan. J Pak Med Assoc. 2015;65(4):380-382.
18. Nadeem A, Cheema MK, Naseer M, Javed H. Comparison of quality of sleep between medical and non-medical undergraduate Pakistani students. J Pak Med Assoc. 2018;68(10):1465-1470.
19. Rezaei M, Khormali M, Akbarpour S, Sadeghniiat-Hagighi K, Shamsipour M. Sleep quality and its association with psychological distress and sleep hygiene: a cross-sectional study among pre-clinical medical students. Sleep Sci. 2018;11(4):274-280. doi: 10. 5935/ 1984-0063.20180043.
20. Ibrahim NK, Badawi FA, Mansouri YM, Ainousa AM, Jambi SK, Fatani AN, et al. Sleep Quality among Medical Students at King Abdulaziz University: A Cross-sectional Study. J Community Med Health Educ. 2017; 7: 561. DOI: 10.4172/2161-0711.1000561
21. Alsaggaf MA, Wali SO, Merdad RA, Merdad LA. Sleep quantity, quality, and insomnia symptoms of medical students during clinical years: relationship with stress and academic performance. Saudi Med J 2016;37:173–82
22. Surani AA, Zahid S, Surani A, Ali S, Mubeen M, Khan RH. Sleep quality among medical students of Karachi, Pakistan. J Pak Med Assoc. 2015;65(4):380-382.
23. Nadeem A, Cheema MK, Naseer M, Javed H. Comparison of quality of sleep between medical and non-medical undergraduate Pakistani students. J Pak Med Assoc. 2018;68(10):1465-1470.
24. Lohitashwa, R., Kadli, N., Kisan, R., A, S., & Deshpande, D. Effect of stress on sleep quality in young adult medical students: a cross sectional study. International Journal of Research in Medical Sciences. 2017; 3(12), 3519-3523. doi:10.18203/2320-6012.ijrms 20151391
25. Young DR, Sidell MA, Grandner MA, Koebnick C, Troxel W. Dietary behaviors and poor sleep quality among young adult women: watch that sugary caffeine! Sleep Health. 2020;6(2):214-219. doi: 10.1016/ j.sleh. 2019.12.006

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FI, ARA: Conceptualization of Project
ARA: Data Collection
MAN, RKA: Literature Search
HS, AA: Drafting, Revision
ARA, RKA: Writing of Manuscript

Cephalic Index of Students of Sialkot Medical College

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Abstract

Objective: The aim of study was to find out cephalic index of the students of Sialkot medical college. It will help in identification.

Method: Only students of Sialkot medical college were selected by non-probability purposive sampling technique. Sample size was 141. Both males and females were selected. Study setting was Sialkot medical college, Sialkot. Duration of study was one month. After taking informed consent measurements were taken i.e., from mastoid to mastoid and from glabella to external occipital protuberance. The measurements were taken in centimeters. Frequency and percentage was calculated by using SPSS 21. Graphs and table were formed.

Results: The results indicate that most of the students were hyperbrachycephalic. Hyperbrachycephalic were predominant with 63 %, 94.5 and 43.8 % for collective, male and female respectively. Mesaticephalic were 11%,0% and 18% in both sexes, males and females respectively. Brachycephalic were 26%, 5.5% and 38.2% for both sexes, males and females respectively.

Conclusion: This study indicates that cephalic index of most of students was hyperbrachycephalic. Males predominantly belong to hyperbrachycephalic group. While in females hyperbrachycephalic group predominated then brachycephalic.

Keywords: anthropometry. mesaticephalic, brachycephalic, hyperbrachycephalic, cephalic index.

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Introduction

Cephalic index has been described in late sixteenth and early seventeenth century in Sweden. Retzius derived a formula by multiplying hundred with span between the most extending focuses along the edges of the head, above and behind the ears. Then dividing the outcome with measurement from the craniometric point to the most extending point at the rear of the head.[1]

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When this formula is applied to the head dimensions of alive one it is called cephalic index but when such dimensions are taken in dead ones head without soft tissues then it will be named cranial index.[2]

Measurements of different body parts have long been used to individualize the person.[3] Among those head measurements also provide useful data to differentiate on the basis of race. Race is a significant idea and boundary to contemplate people in light of the fact that every one of them are unique. Race is a natural idea identified with actual qualities as opposed to mental characteristics or interaction of people while living in a community.[4]

Cephalic index is not only utilized to differentiate the individuals depending upon the race. It can also be used to differ the males from females. It also provides meaningful information about genetics and environmental effects.[5] In addition, cephalic index can also be used in finding the quality and success of certain cranial operations.[1,6] It has also been used to help the diagnosis

of downs syndrome along with chromosomal defects, age and normal development of fetus.[7]

Based on cephalic file head shapes assembled into four global classifications, that including Dolicocephalic (cephalic index less than 74.9), which is derived from Greek word meaning long and dainty head. Brachycephalic (cephalic index 80 to 84.9), meaning small and wider. Mesatocephalic (cephalic index 75 to 79.9), meaning moderately long and broader, and Hyperbrachycephalic (cephalic index 85 to 89.9), extremely small and wider and ultra-brachycephalic (cephalic index more than 92) .[2,7-10]

Various elements have been proposed to conceivably affecting the head structure. In addition to inborn elements, protein intake, stress, provision of medicine in the hour of need and climatic changes.[11] So inhabitants of different geographical areas may show different cephalic index. This study will help to find out the cephalic index of students of Sialkot medical college.

Material and Methods

The study setting was Sialkot medical college. Sample size was 141. Sampling technique was non probability purposive sampling. Both males and females were selected. 54 were males and remaining were females. It was a cross sectional study. Study duration was one month. After taking informed consent measurements were taken by caliper. From glabella to the external occipital extension and from parietal extension of one side to the other were measured. Measurements were taken in centimeters. Head breadth was multiplied to 100 and divided to head length. Frequency and percentage was calculated by using SPSS 21. Graphs and table were formed.

Results

There were 141 students whose measurements were taken and cephalic index was calculated. Their results are being shown in table no 1. It indicates that mean cephalic index in males was 93.91 and in females it was 102. Frequency of different values was plotted in the graph as shown in figure no 1, for males and figure no 2 for females.

Table 1: *Descriptive data.* **Descriptive Statistics**

	N	Range	Minimum	Maximum	Mean
Male_CI	54	21.00	81.00	102.00	93.9130
Female_CI	87	38.26	76.74	115.00	90.3861

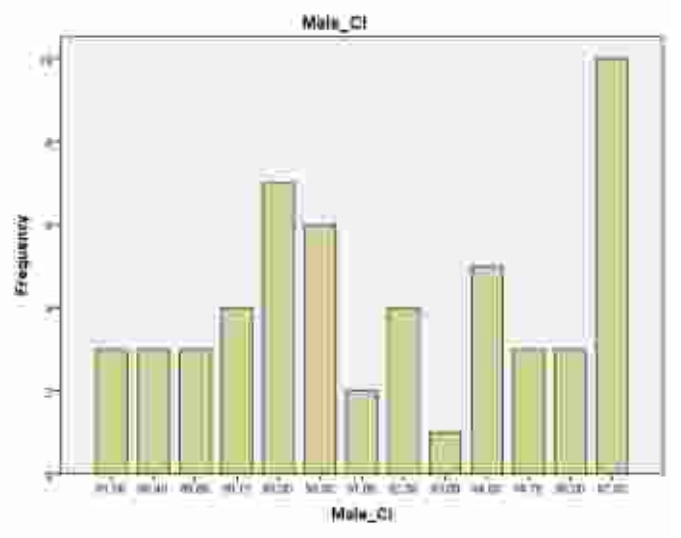

Figure No 1: *Frequency of different cephalic indices for males.*

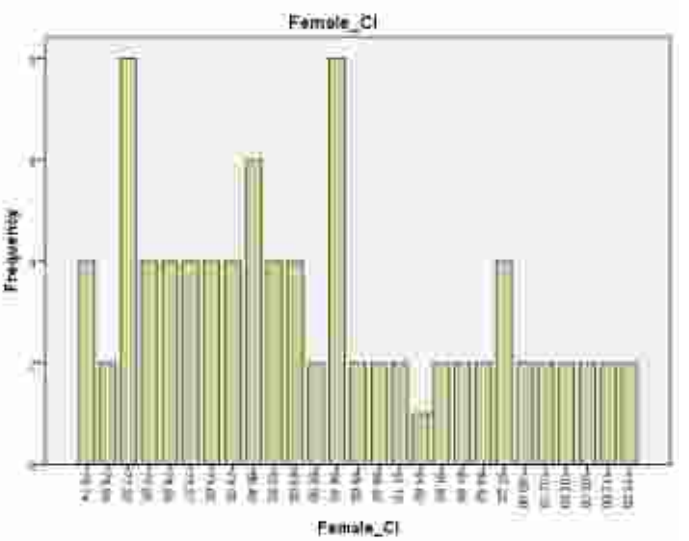

Figure No 2: *Frequency of different cephalic indices for females.*

Table 2: *Percentage of different racial groups depending upon C.I.*

		Dolicho-cephalic	Brachy-cephalic	Mesati-cephalic	Hyperbra-chycephalic
Male	Number	---	3	---	51
	%age	---	5.5	----	94.5
Female	Number	----	34	16	39
		----	38.2	18	43.8
Both	Number	----	37	16	90
	% age	-----	26	11	63

Discussion:

The results indicate that most of the students were hyper-

brachycephalic. Hyperbrachycephalic were predominant with 63 %, 94.5 and 43.8 % for collective, male and female respectively. Mesaticephalic were 11%,0% and 18% in both sexes, males and females respectively. Brachycephalic were 26%,5.5% and 38.2% for both sexes, males and females respectively.

In a study carried out in Japan 68 were ultra-brachycephalic and 305 hyperbrachycephalic.[8] In a study in India shows that the hyperbrachycephalic constituted only 6% and 33% of brachycephalic. In boys, the dominating group was brachycephalic with dolichocephalic but in girls dominating group was brachycephalic but hyperbrachycephalic were 29%.[12] A study carried out in Nigeria, it was deducted that dolichocephalic were the most of all. The least was hyperbrachycephalic with 1%. Brachycephalic were 10.23%.[9] In India in another study, in boys the predominant group was mesaticephalic and in girls brachycephalic was leading group.[13] In Odhiya Pradesh, a study carried out indicated that mesocephalic were dominating in boys and least were hyperbrachycephalic with only 1 percent. In girls brachycephalic were more than boys and hyperbrachycephalic were same[14]. There were no brachycephalic in boys but twelve percent in girls. Dolichocephalic and mesaticephalic were dominating, in another study carried out in India.[15] In Japan, ultrabrachycephalic were 78, 378 hyperbrachycephalic and maximum were brachycephalic.[11] A study carried out on Punjabi students indicated that the predominant group was hyperbrachycephalic[16]. In another research done in Malaysia, it was found that Indians were hyperbrachycephalic and brachycephalic. The Chinese were hyperbrachycephalic and Malaysian were mesocephalic.[17]

A study carried out in Pakistan indicated that the predominant group was hyperbrachycephalic along with brachycephalic in both sexes. Dolichocephalic were found to be zero percent. Same results were found in Iran (Qazvin).[18] In Iran, brachycephalic and hyperbrachycephalic were found main groups of cephalic index.[19] The results of this study were contradicting another study performed in Pakistan on skulls which indicated that dolichocephalic were predominant.[20] The cranial measurements help to find out skull anatomical anomalies. These measurements can be taken with cheap and easy to use measuring instruments. To clear the measuring error, it can be taken multiple times.[21] Due to crossbreeding of races, results of this study show mixture of various types of cranial indexes which is also seen in many other studies.[22-25]

Conclusion

This study indicates that cephalic index of most of students was hyperbrachycephalic. Males predominantly belong to hyperbrachycephalic group. While in females hyperbrachycephalic group predominated then brachycephalic.

Conflict of Interest: *None*

Referrences

1. Van Lindert EJ, Siepel FJ, Delye H, Ettema AM, Bergé SJ, Maal TJ, et al. Validation of cephalic index measurements in scaphocephaly. Child's nervous system. 2013;29(6):1007-14.
2. Kumar A, Nagar M. Morphometric estimation of cephalic index in north Indian population: craniometrics study. International Journal of Science and Research. 2015;4(4):1976-82.
3. Khatun S. Cephalic index in indigenous Tharu community. J Nepal Med Assoc. 2018;56(213):825-9.
4. Primasari A, Ria N, Sutadi H. Vertical cephalic index, dental arch and palatal depth measurement: A study in Bataknese children. Pesquisa Brasileira em Odontopediatria e Clínica Integrada. 2019;19.
5. Kumar M, Gopichand PV. The study of cephalic index in Haryanvi population. Int Jr of Pure and Appl Biosc. 2013;1(3):1-6.
6. Marcus JR, Domeshek LF, Das R, Marshall S, Nightingale R, Stokes TH, et al. Objective three-dimensional analysis of cranial morphology. Eplasty. 2008;8.
7. Mohammed MY, Ugwu Anthony C, Modu AA, Mohammed A. Sonographic Assessment Of Foetal Cephalic Index Among The Fulanis In Maiduguri, Borno State.
8. Hossain MG, Sabiruzzaman M, Islam S, Ohtsuki F, Lestrel PE. Effect of craniofacial measures on the cephalic index of Japanese adult female students. Anthropological Science. 2010;118(2):117-21.
9. Eroje M, Fawehinmi H, Jaja B, Yaakor L. Cephalic index of Ogbia tribe of Bayesla state. Int J Morphol. 2010; 28(2):389-92.
10. Eze CU, Ene DC, Abonyi LC, Omiyi DO. Normal value of cephalic index and craniotypes: a pilot sonographic cephalometric survey of pregnant women of Yoruba ethnic origin in Lagos, southwest Nigeria. South African Radiographer. 2018;56(2):26-31.
11. Hossain MG, Saw A, Alam R, Ohtsuki F, Kamarul T. Multiple regression analysis of anthropometric measurements influencing the cephalic index of male Japanese university students. Singapore Med J. 2013; 54(9): 516-20.

12. Yagain VK, Pai SR, Kalthur SG, Chethan P, Hemalatha I. Study of cephalic index in Indian students. Int J Morphol. 2012;30(1):125-9.
13. Kumari KL, Babu P, Kumari PK, Nagamani M. study of cephalic index and facial index in Visakhapatnam, Andhra Pradesh, India. 2015.
14. Patro S, Sahu R, Rath S. Study of cephalic index in Southern Odisha population. IOSR J Dent Med Sci. 2014;13:41-4.
15. Salve VM, Thota NR, Patibandla A. The study of cephalic index of Andhra region (India). Asian Journal of Medical Sciences. 2011;2(1):53-5.
16. Mahajan A, Khurana BS, Batra APS. The study of Cephalic index in Punjabi students. 2009.
17. Attalla SM, Deri NM. Racial identification of head shape by the cephalic index in the malaysian population in section 13 Shah Alam Malaysia. International Journal of Medical Toxicology & Legal Medicine. 2018; 21(3 and 4):8-10.
18. Hassanzadeh G, Sadr M, Alaghbandha N, Dehbashipour A, Abbas MA, Heydar Zeidi O. Anthropometric characteristics of craniums in residents of Qazvin, Iran and Dera Ghazi Khan, Pakistan: A comparative study. Anatomical Sciences Journal. 2013;10(1):43-9.
19. Madadi S, Khanehzad M, Tahmasebi F, Gordon K, Hassanzadeh G. Correlation of horizontal cephalic index and cranial parameters in Iranian medical students. Acta Medica Iranica. 2018:577-84.
20. Anwar Saood S, Quddus UR. Significance of cephalic index in race determination. 2012.
21. van Lindert EJ, Siepel FJ, Delye H, Ettema AM, Bergé SJ, Maal TJ, Borstlap WA. Validation of cephalic index measurements in scaphocephaly. Child's nervous system. 2013 Jun 1;29(6):1007-14.
22. Chakrabarti JS, Choudhury P, Chakraborty PN. A study of cephalic index of Bengali subjects of Tripura for determination of race. Journal of Medical Society. 2018 May 1;32(2):91.
23. Kyei G, Moshkdanian G, Pasbakhsh P, Abolhasani F, Rastegar T, Hassanzadeh G. Cephalofacial characteristics of the Akan people in the Assin Districts in Central Region of Ghana: Anthropometric Studies. Journal of Contemporary Medical Sciences. 2020 Apr 11;6(2).
24. Anjum MI, Kanwal S, Anjum MI. A craniometric study of adult dry skulls in South Punjab. Pak. J. Med. Health Sci. 2016 Jan 1;10(1):244-6.
25. Alves HA, Santos MI, Melo FC, Wellington R. Comparative Study of the Cephalic Index of the Population from the Regions of the North and South of Brazil. Int J Morphol. 2011 Dec 1;29(4):1370-4.

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MA: Conceptualization of Project
GM: Data Collection
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YA: Drafting, Revision
AA, MA: Writing of Manuscript

Work Motivation and Job Satisfaction among Young Doctors of Public Health Sector in Punjab, Pakistan

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Abstract

Objective: To assess determinants of job satisfaction and work motivation of doctors working in the largest tertiary care hospital of Pakistan.

Method: A cross-sectional study was conducted using mixed methods. The Warr, Cook, and Wall's Job Satisfaction Scale (JSS) instrument was used for data collection. The quantitative sample size comprised 85 doctors, while the in-depth interviews (IDIs) were carried with 15 doctors for the qualitative portion. Chi-square Test (x2) was used with the p-value set at ≤0.05 for significant findings. Thematic content analysis was done to analyse the qualitative data.

Results: Overall, the results showed a higher level of job satisfaction and work motivation in senior doctors. It was also associated with 'place of residence', 'financial incentives', 'department category' including 'level of gratitude by patients', etc. In qualitative analysis, the major themes that were highlighted were the 'role of government policies', 'working conditions', 'cumbersome administrative requirements', 'inadequacies in graduate training', 'monetary gains' , 'role of media', 'Bribe (Safaris)', and lastly 'sense of security'.

Conclusion: The study demonstrates an overall low level of job satisfaction and work motivation in young doctors in the PHS. The introduction of unfavourable government policies, the lack of a solid healthcare skeleton, disparaging working conditions and the negative portrayal of the young doctors by the media seem to be the most critical underlying factors.

Keywords: Work Motivation, Job Satisfaction, Public Health Sector, Pakistan.

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Introduction

The health workforce is unequivocally one of the most fundamental components of the health system, which has a strong bearing on the overall performance of the health system.[1] According to World Health Organization (WHO), there are approximately 59.2 million health providers working around the globe, and a shortage of almost 4.3 million physicians, midwives, nurses, and support workers[2] that would ultimately widen to 12.9 million roughly by 2035.[3] Pakistan is a lower-middle country with a population of 216.5 million, as reported in 2019.[4] The country has been categorized by WHO as one of the 57 countries[2] facing an acute shortage of physicians needed to deliver essential health interventions for achieving Universal Health Coverage (UHC). Pakistan has one of the lowest densities of health workers in the region and globally, with an essential /skilled health professional (physicians including specialists, nurses, lady health visitors (LHVs) and midwives) density of 1.4 per 1,000 population,[5] which is far below the minimum threshold of 4.45 per 1000 population necessary to achieve UHC.[6]

Work motivation and job satisfaction have been identified as one of the key factors of health worker retention and turnover in low- and middle-income countries (LMICs).[7,8,9] Work motivation and job satisfaction are

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complementary but distinct entities affecting the performance of health workers as attributed by a cross-sectional study conducted at primary health facilities in Nepal.[10]

According to Locke, job satisfaction is defined as a positive emotional state, resulting from the appraisal of one's job or job experiences.[11] Job satisfaction improves retention and is achieved by improving working conditions, participation in decision making, and management as well as professional development.[12] Motivation can be defined as an individual's degree of willingness to exert and maintain an effort to achieve personal and organizational goals.[13,14] Although neither job satisfaction nor motivation is directly discernible, they are critical to the retention and performance of health workers.[13,15]

A large body of literature analyses the notions of job satisfaction and work motivation and their relationship with turnover intention and actual physician migration.[16,17] A report from British National Health Service (NHS) pertaining to nurses highlights how the NHS is losing its workforce to the market due to higher opportunities for career development and better promotion prospects.[18]

A study from Serbia reports that out of 170 health care workers employed in rehabilitation centres, only 22.4% were content with their jobs, causes of dissatisfaction were the work environment, lack of autonomy and not being part of the decision-making processes.[19] A study from Norway reports good leadership, feedback, and support from seniors were key factors for workers' job satisfaction.[20] A study to assess job satisfaction among nurses in Pakistan showed that 86 percent of respondents were dissatisfied with their jobs; citing poor working conditions, lack of privileges, respect in their workplace, and time pressure being mainly responsible.[21] Another study conducted in two medical colleges of Pakistan reported that more than 50 percent of the students intended to leave the country after their graduation due to the low quality of training as well as salary structure, and poor teaching standards in local teaching hospitals.[22]

The present study was conducted to assess determinants of job satisfaction and work motivation of doctors working in the largest tertiary care hospital in Pakistan. The findings will provide policy recommendations that could improve the current situation in order to reduce the attrition of trained professionals from Pakistan.

Material and Methods

A cross sectional study using mixed methods with both quantitative questionnaires and qualitative in-depth interviews (IDI) was conducted to evaluate the overall level of job satisfaction and work motivation of young doctors. The study setting was Mayo Hospital. The total duration of the study was 3 months.

A sample size of 85 doctors was estimated by using 95% confidence level, absolute precision with expected percentage job satisfaction as 26.7%. The formula applied was $n = Z21\text{-}\alpha/2.p.q / d2$ where $Z21\text{-}\alpha/2$ = confidence level 95% = 1.96% ; p= prevalence; q= 1+p and d = absolute precision 9% . A simple random sampling technique was applied for quantitative methods while purposive sampling was utilized for qualitative methods. The inclusion criteria specified that the doctors had graduated within the recent five years, were MBBS graduates and belonged to the government sector only, PHS. While exclusion criteria curtailed that doctors not in active clinical practice and those belonging to AHS, DPT, BDS and other disciplines were not be included.

The instrument used for data collection was The Warr, Cook, and Wall's Job Satisfaction Scale (JSS).[23] The factors highlighted different dimensions and nature of the 16 items in the survey. The IIP Scale (Inventory of Interpersonal Problem) was used for the establishment of response options of the questionnaire with[1] extremely dissatisfied to[7] extremely satisfied.

The key factors explored for assessing work satisfaction were broadly classified into two categories: general factors and specific factors. The demographic variables included 'gender', 'age', 'specialty', 'shift workload', 'boredom', 'danger', 'control', 'job security', and 'monetary compensation'. Consequently, the specific factors measured were 'amount of sleep', 'worry and stress', 'financial problems', plus 'room for development and growth'. Similarly, the constructs gauging motivation were grouped into two broad categories outlining "Positive motivating factors" and "demotivating factors". The variables focused mainly on the factors of 'drive', 'control', 'challenge', 'relationships', and 'incentive of reward'. 10 doctors were chosen for pilot testing the questionnaire.

Qualitative data collection was done to explore the doctor's perceptions regarding job satisfaction and work motivation determinants in Mayo Hospital. The research team conducted IDIs with 15 doctors. Those

who agreed to participate were included in the study. A predetermined, open-ended topic guide was used for discussions with the doctors, to allow each participant to respond in a way that reflected their insights and opinions. The data was collected until saturation in responses was achieved. Comprehensive transcripts were developed from the recordings and field notes for analysis while listening to the audiotapes. Numerous factors were identified, condensed, and then coded. Codes were then clustered together and categories followed by sub-categories were created. The categories were then merged and the main theme was identified.

Verbal consent was obtained from all participants before conducting data collection. Ethical approval was duly obtained from the Institutional Review Board of the university.

Table 1: *The table shows the demographic details of the quantitative study sample of 85 doctors who were administered the questionnaire for accessing job satisfaction and work motivation.*

Demographic	Sub-division	% (Frequency)
Gender	Male	63.5% (54)
	Female	36.5% (31)
Year of Graduation	2012	7% (6)
	2013	17.6 % (15)
	2014	17.6% (15)
	2015	16.5 % (14)
	2016	43.5% (37)
Institute of graduation	Government college	88.2 % (75)
	Private College	9.4 % (8)
	Abroad	2.4 % (2)
Marital status	Married	77.6 % (66)
	Unmarried	22.4% (19)
Place of Origin	Punjab	90.5 % (77)
	Azad Jammu Kashmir	7.1 % (6)
	Gilgit Baltistan	1.1 % (1)
	Others	1.1% (1)
Hospital Department	Medicine	42.3 % (36)
	Surgery	32.9% (28)
	Paediatrics	16.5% (14)
	Others	8.2 % (7)

Results

The quantitative variables in the study were all nominal and so the chi square (x^2) test was used with the p-value set at ≤0.05 for significant findings. IBM SPSS Statistics was used to derive the results.

The dependent variables were work motivation and job satisfaction. The data showed higher levels of work motivation and job satisfaction in senior doctors due to better workplace relationship with nurses (p-value = 0.02) as compared to recent graduates who faced more problems while interacting with the paramedical staff.

Results revealed that graduates from outside of Lahore were more satisfied with their bonus and wages as compared to doctors practicing in the centre as a strong correlation was found between 'place of origin' and 'chances of receiving a bonus' (p-value=0.05).

'Department category' and 'workplace harassment' (p-value=0.01), had a strong correlation with work motivation and job satisfaction as many lady doctors belonging to the surgical departments reported an overall chauvinistic vibe of a 'men's club'.

Furthermore, doctors training in Allied health departments (paediatrics, dermatology, anaesthesia, cardiology) showed increased work motivation as there was a higher percentage of gratitude shown by the patients, as emphasized by the strong correlation between 'department' and 'feedback and gratitude shown by the patients' (p-value=0.03).

A significant negative correlation was found between 'year of graduation' and 'finding the work stimulating and challenging' (p-value=0.05) respectively, underlining the recently graduated doctors lacked a substantial amount of job satisfaction in comparison to senior doctors with the overall satisfaction dwindling each year.

Additionally, a non-significant chi- square test was found between 'marital status' and 'fringe benefits' (p-value=0.07), translating to doctors settled with families had a preference for training jobs offering additional benefits such as health insurance, provident trust, housing/utilities fund, and paid leaves (i.e., fringe benefits).

In Qualitative analysis of the research, the major themes were prioritized with reference to number of repetitions in the IDIs. In descending order of importance, the major underlying determinants for job satisfaction and work motivation are presented.

Introduction of new government policies/ Central Induction Policy (CIP)

The foremost theme was regarding the introduction of novel government policies/CIP by the respondents. Since 2016, in order to get a residency in Govt. Institutes of Punjab, candidates need to apply in Punjab Residency

Table 2: *The table below summarizes all the major themes derived from the qualitative portion of the study*

Major theme	Description
Introduction of new government policies	Refers to Central Induction Policy (CIP) that was put into effect in 2016 regarding the post-graduate training of public health sector doctors.
Working conditions	Infrastructure plus overall facilities, their quality and adequate provision both in hospitals and for medical staff.
Cumbersome administrative requirements	Lack of a proper, administrative setup for both post-graduate training and hospital.
Inadequate post-graduate training	Refers to the absence of learning opportunities or slots being available to pursue all specialties.
Monetary gains	The pay to workload ratio.
Ability to make a 'difference'	Doctor's personal sense of contentment from delivering services to people from a perspective based on humanitarian grounds.
Family Support	In terms of both emotional support and provision of funds foreducation.
Role of media	Television channels and social network's portrayal of public health services in general.
'Bribe/ *Sifaarish*'	Nepotism, favouritism or connections providing some undue favour.
Sense of security	Both in terms of doctor's job and physical security from workplace harassment.

Program (PRP)/ CIP, which sets a merit incorporating post-graduate exams, undergraduate performance in professionals and distinctions, research, house job and work experience in peripheral areas of Punjab such as Basic Health Unit (BHU) and Rural Health Centres (RHC). Upon the basis of a calculated merit, the doctors are inducted into training throughout Punjab into their preferred specialties, depending on the availability of seats.

"Since the introduction of CIP, I think the future is pretty bleak for post-graduate training in Pakistan so we have to avail other options elsewhere, looking at the other choices like PLAB (The Professional and Linguistic Assessments Board) or USMLE (United States Medical Licensing Exams)".

"CIP has created a panic situation amongst the young doctors", were some of the remarks given by the majority of the respondents on recent government policies.

According to the respondents, there was discrimination and partiality in the process of allocation of seats. They highlighted their concerns regarding working in BHUs and RHCs as according to them acquiring job slots in the periphery had become increasingly dependent on connections and "sifaarish". After CIP, due to a steep decline in the number of post-graduate training seats, longer specialization period, and other hurdles placed in the path of specialization, the data highlighted that there is an evident sense of insecurity among the doctors regarding their futures. Many doctors are inducted through CIP into fields other than the ones they preferred due to a lack of seats in most specialties of their choice.

Lack of a conducive working environment

Secondly, lack of a conducive working environment was another very important theme that emerged in the qualitative data analysis.

One participant is reported to have said, "Doctor's own life, their health, their security is at stake…I believe that people who are working here are bound to work here due to their own problems and issues otherwise no one would opt for such conditions."

Another participant emphasized on the lack of adequate facilities in peripheral areas as she said, "What would anyone do in a BHU? What if a cardiac patient comes? All you have is the ECG, then what?"

Regarding the workload an interviewee explained that in a surgical outdoor setting one was expected to see 10-15 patients per House Officer (HO), within a span of 5 hours. During the "ward week" of an HO is expected to look after around 10 indoor patients round the clock, minus a few duties.

A post-graduate trainee (PGR) with experience in multiple hospital settings revealed how "From OPD (outpatient department) to surgeries, Mayo Hospital has the highest number of patients in all hospital I've worked in so far."

A few participants pointed out that many cases could have been dealt within BHUs and RHCs had they been better equipped and patients would not have to travel from far-flung villages.

"I really feel sorry for them when they are crying for basic needs like oxygen cylinders or endotracheal tubes, and even the ECG machines don't work".

Cumbersome administrative requirements

Cumbersome administrative requirements appeared strongly as another theme. The doctors encounter countless hurdles, as one HO recalled, in the shape of "meaningless paperwork" while applying for house job even if they are the graduates of the "parent institute".

One HO noted that there are two systems for postgraduate training MD/MS (Doctor of Medicine/Doctor of Surgery) and FCPS (Fellow of College of Physicians and Surgeons) and implored, "Make matters easy for us! But they are not doing that. So, basically you are pushing us to get out." Another house officer also said exasperatedly, "What advancement opportunities? Do you see any?"

Inadequacies in professional training

A few respondents pointed out that shortfalls in professional training led to deteriorating job satisfaction and work motivation amongst them. They agreed that the prescribed curriculum focuses more on theoretical knowledge rather than practical.

A house officer joked light-heartedly, "We could have learned how to pass a Foley catheter but they taught us how to make small packets in Pharmacology."

Monetary gains

Monetary gains were considered a compelling factor leading to a decreased work motivation and job satisfaction in young doctors. Most of the respondents said that an HO's salary was sufficient as long as they do not have a family to but the salary received by PGRs was considered inadequate.

Contentious role of media

Regarding the controversial role of media in the negative portrayal of the doctors' community, all the respondents unanimously agreed that the media is propagating an antagonistic and hostile image of healthcare providers without probing the root problems that compels the young doctors to protest and go on strikes.

"Maseeha qatil ban gaye" (saviours turned into killers) being one of the favourite phrases of the respondents, also included other remarks such as: "Doctors have been victimized badly.",," The reporters will broadcast the news that will sell", "No matter what the issue is they blame the young doctors!".

A few respondents verbalized that such negative media campaigns have adversely affected doctors' image in the general public leading to erosion of respect that was a fundamental factor in motivating doctors in the public service. Few believe that this has led to an irreversible damage and has drastically transformed how the society views and treats doctors, thus dwindling motivation levels of the doctors and enhancing the abjection to the system.

"I feel like I'm not doing something right and there will always be a certain prejudice from now on," an HO commented.

Workplace harassment

Additionally, some women doctors reported workplace harassment as another underlying factor leading to low job satisfaction and work motivations. "Women in certain wards were expected to arrange food trays and serve food to their male superiors. Male colleagues also misbehave in operation theatres. Many of the male counterparts also have little concept of personal space".

Discussion

Job satisfaction and work motivation are dynamic concepts subject to measurement of multiple variables. The overarching theme of dissatisfaction with government policies and CIP was widely reported. Respondents reported that prior to the introduction of CIP, there was higher chance of young graduates securing residency seats in their preferred specialty within their parent institute affiliated hospital. Now, due to the CIP merit system, not only is the route to securing residency tirelessly long, but many doctors are unable to achieve a residency in their preferred specialty due to a fixed number of seats compared to the number of graduates produced each year[24].

The cumbersome process along with the nepotism often faced whilst securing job slots in BHUs and RHCs, has further contributed to the decrease in motivation and job satisfaction amongst healthcare practitioners, which ultimately can lead to the attrition of the medical workforce. Furthermore, the underlying issue of high female doctor dropout[25] after graduation has also mounted due to lack of support and safety concerns in female doctors being sent to practice in the peripheral BHUs and RHCs. A similar study in the UK[18] revealed a substantial effect on job satisfaction of young doctors after government policy changes. The role of media went hand in hand with CIP and the difficult working

conditions as represented in our sample. Outcomes, similar to studies conducted elsewhere, demanded improvement in monetary benefits,[9] job structure,[16] and quality of training,[21] and job opportunities.[16]

Most of the respondents felt overwhelmed with the workload[12] and a lack of physical security at the workplace. A similar study done in Iraq showed that the high-turnover intention among doctors was significantly associated with both the working and security conditions.[10]

The hospital environment and the relationship with the nurses and paramedical staff affects the flexibility of the doctor's work life and affects their personal life.[5] It is imperative to state that majority of the factors are modifiable such as doctor's pay scale, promotional infrastructure and working conditions as mentioned in a study conducted in 18 national hospitals in Ugandan.[8] A similar study in Fijis School of Medicine highlighted the impact of lack of training opportunities, financial factors, poor working conditions on career decision making process as well.[16]

Conclusion

The study demonstrates an overall low level of job satisfaction and work motivation in young doctors in the PHS. The introduction of unfavourable government health-sector policies that hinder growth of the young doctors, lack of a solid healthcare skeleton, disparaging working conditions and the negative portrayal of the young doctors by the media seem to be the most critical underlying factors.

Conflict of interest: *None*

References

1. Global Health Workforce Alliance [GHWA] (2008) Scaling up, Saving Lives. Task Force for Scaling up Education and Training for Health Workers. WHO, Geneva. - References - Scientific Research Publishing [Internet]. [cited 2022 Jun 22]. Available from: https://www.scirp.org/%28S%28vtj3fa45qm1ean45vvffcz55%29%29/reference/referencespapers.aspx?referenceid=1266881
2. Guilbert JJ. The World Health Report 2006: working together for health. Educ Health Abingdon Engl. 2006 Nov;19(3):385–7.
3. WHO | Global health workforce shortage to reach 12.9 million in coming decades [Internet]. WHO. World Health Organization; [cited 2022 Jun 22]. Available from: https://apps.who.int/mediacentre/news/ releases/2013/health-workforce-shortage/en/index.html
4. Fact sheet: The International Development Association (IDA) [Internet]. World Bank. [cited 2022 Jun 22]. Available from: https:// www. worldbank. org/en/ news/factsheet/2019/12/13/fact-sheet-the-international-development-association-ida
5. World health statistics 2017: monitoring health for the SDGs, sustainable development goals [Internet]. [cited 2022 Jun 22]. Available from: https:// www. who. int/publications-detail-redirect/9789241565486
6. Global strategy on human resources for health: Workforce 2030 [Internet]. [cited 2022 Jun 22]. Available from: https://www.who.int/publications-detail-redirect/9789241511131
7. Willis-Shattuck M, Bidwell P, Thomas S, Wyness L, Blaauw D, Ditlopo P. Motivation and retention of health workers in developing countries: a systematic review. BMC Health Serv Res. 2008 Dec 4;8:247.
8. Buwembo W, Munabi IG, Galukande M, Kituuka O, Luboga SA. A qualitative analysis of health professionals' job descriptions for surgical service delivery in Uganda. Hum Resour Health. 2014 May 12;12(Suppl 1):S5.
9. Adzei FA, Atinga RA. Motivation and retention of health workers in Ghana's district hospitals: addressing the critical issues. J Health Organ Manag. 2012; 26(4–5): 467–85.
10. Work motivation and job satisfaction among health workers at primary health facilities: a cross-sectional study from Nepal [Internet]. 2020 [cited 2022 Jun 22]. Available from: https://www.researchsquare. com
11. Locke E. The Nature and Causes of Job Satisfaction. Handb Ind Organ Psychol. 1976 Jan 1;31.
12. Franco LM, Bennett S, Kanfer R. Health sector reform and public sector health worker motivation: a conceptual framework. Soc Sci Med 1982. 2002 Apr; 54(8): 1255–66.
13. Dolea C, Adams O. Motivation of health care workers-review of theories and empirical evidence. Cah Sociol Demogr Med. 2005 Mar;45(1):135–61.
14. Henderson LN, Tulloch J. Incentives for retaining and motivating health workers in Pacific and Asian countries. Hum Resour Health. 2008 Sep 15;6(1):18.
15. Harnmeijer J. Improving health worker performance: in search of promising practices. 2000 Jan 1 [cited 2022 Jun 23]; Available from: https://www.academia.edu/32394274/Improving_health_worker_performance_in_search_of_promising_practices

16. Steinmetz S, de Vries DH, Tijdens KG. Should I stay or should I go? The impact of working time and wages on retention in the health workforce. Hum Resour Health. 2014 Apr 23;12:23.
17. Peters DH, Chakraborty S, Mahapatra P, Steinhardt L. Job satisfaction and motivation of health workers in public and private sectors: cross-sectional analysis from two Indian states. Hum Resour Health. 2010 Nov 1;8:27.
18. Allen L. I. Seccombe and G. Smith, Taking Part: Registered Nurses and the Labour Market in 1997, Brighton: Institute for Employment Studies, 1997, £25.00, Report No. 338. Work Employ Soc. 1998 Dec;12(4):811–2.
19. Jovic-Vranes A, Bjegović-Mikanović V, Boris V, Natasa M. Job satisfaction in Serbian health care workers who work with disabled patients. Open Med. 2008 Jun 1;3:221–4.
20. Krogstad U, Hofoss D, Veenstra M, Hjortdahl P. Predictors of job satisfaction among doctors, nurses and auxiliaries in Norwegian hospitals: relevance for micro unit culture. Hum Resour Health. 2006 Feb 1;4:3.
21. Bahalkani HA, Kumar R, Lakho AR, Mahar B, Mazhar SB, Majeed A. Job satisfaction in nurses working in tertiary level health care settings of Islamabad, Pakistan. J Ayub Med Coll Abbottabad JAMC. 2011 Sep; 23 (3): 130–3.
22. Syed NA, Khimani F, Andrades M, Ali SK, Paul R. Reasons for migration among medical students from Karachi. Med Educ. 2008;42(1):61–8.
23. Warr's Job Satisfaction Scale (WJSAT) [Internet]. [cited 2022 Jun 23]. Available from: https:// scales. arabpsychology. com/s/warrs-job-satisfaction-scale-wjsat/
24. PHF - Punjab Health Foundation [Internet]. [cited 2022 Jun 23]. Available from: https:// www. phf.gop. pk/ about_core_team_page.html
25. Junaidi I. 50pc of female doctors never work after graduation [Internet]. DAWN.COM. 2014 [cited 2022 Jun 23]. Available from: http://www.dawn.com/ news/ 1139557

Authors Contribution

HT, ST: Conceptualization of Project
HT, MM, ZA, UA: Data Collection
ASB, MM, UA: Literature Search
ST, MM, ZA: Statistical Analysis
HT, ST: Drafting, Revision
ST, ST, ASB: Writing of Manuscript

Comparison of Efficacy Between Intralesional Traimcinolone and Platelet Rich Plasma in the Treatment of Alopecia Areata

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Abstract

Objective: The aim of the research is to compare the efficacy of intralesional triamcinolone acetonide and PRP (platelet rich plasma) in the management of Alopecia Areata (AA).

Methods: A total of 180 patients, 18 years and above of both genders were involved in this research after getting approval from hospital ethical committee. Patients were enrolled through OPD of Dermatology Department /AMC/LGH Lahore. The global AA severity score "Severity of Alopecia Tool" (SALT), which relies over the extent and density of scalp baldness and evaluated through two investigators, was used. Patients were randomly assigned into 2 groups: All cases were randomized into 2 treatment groups utilizing computer generated random number table. Group-A received Triamcinolone acetonide (TA) (10 mg/ml) and Group-B received PRP. The data was analyzed through SPSS version 22.

Results: The patient average age was 36.02 ± 12.20 years with minimum and maximum age group. The average age of cases in TA group was 35.39 ± 12.12 years ranging from 18 to 68 years and average age in PRP group was 36.64 ± 12.32 years ranging from 18 to 68 years. In this study there were 109(60.56%) male and 71(39.44%) female cases with 1.59:1 male to female ratio. In TA group there were 59(65.56%) males and 31(34.44%) females and in PRP group there were 50(55.56%) males and 40(44.44%) female cases. In TA group 37(41%) of patients had complete resolution while 53(58.9%) of the cases did not have complete resolution. In PRP group 44(48.9%) of the patients had complete resolution and 46(51.1%) of the patients did not have complete resolution. The complete resolution was statistically same in PRP group in comparison with TA group, p-value = 0.294 i.e. > 0.05.

Conclusion: It is concluded that the use of PRP is associated with higher frequency of complete resolution than intralesional TA, but it was not statistically significant. So, keeping in mind higher cure rate, PRP injection can be used for treatment of AA because it is an easy, feasible and cost-effective treatment option.

Keywords: Alopecia areata, intralesional triamcinolone acetonide, platelet rich plasma, SALT score.

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Introduction

Alopecia areata (AA) is a type of autoimmune hair loss affecting the teenagers and adults. It can occur in patches, diffuse or intersecting patterns. Prevalence of AA is around 2% in the world. It doesn't recognize genders but it is found to be more prevalent in females.[1] Prevalence may be affected by population contemplated like in Turkey and India, most of cases relate to men which exhibit extreme form in contrast to females (63% versus 36% separately). It usually begins in the 3rd and 4th decades of life but may occur at any age.[2] Disease occurring in earlier age has more prolonged and wide-

spread course. About 1 to 2% of patients, the disease can extend to the whole scalp known as Alopecia totalis or to the whole skin known as Alopecia universalis.[3]

Hair loss in AA develops due to antibodies which influence the hair follicles in the anagen phase, explicitly, CD4+ and CD8+ lymphocytes penetrate the hair bulb. CD8+ is mostly involved in destroying follicle found in early disease, while CD4+ involved in the progression of disease.[4]

Alopecia areata generally manifested as an abrupt hair loss occurring typically in a round or oval patches. The most well-known site influenced by AA is scalp in 90% of cases but rest of body hairs like eyelashes, eyebrows, whiskers, underarm, and pubic hair may also be affected. Exclamation point hairs might be observed inside or nearby alopecia patch. Nail manifestations may be present in the form of small pits (30%), trachyonychia (sandpaper nails (10%). Hair loss in alopecia areata is transient and hair have a capacity to regrow as the disease mechanism doesn't permanently destroy hair follicles.[5] Alopecia areata is diagnosed mainly on clinical basis in which age of onset, duration and severity of disorder, positive family history and immune system disorder are considered. Dermoscopy and histopathology are also helpful in follow up and monitoring the response to treatment.[6] Laboratory testing like CBC, serum calcium and thyroid function tests are done to rule out other autoimmune associations.

A quantitative evaluation of scalp balding is done by using Severity of Alopecia Tool (SALT) score in which scalp is allocated in four sections, level of baldness in every section is assessed and multiplied by the area of scalp in percentage.[7]

Long standing AA is quite difficult to manage. Long standing resistant cases may require topical diphenylcyclopropenone, oral immunosuppressants or topical anthralin. It is imperative to screen for psychiatric disturbance attributable to the significant mental impacts of baldness. Intralesional Corticosteroids (ILCs) are taken as pharmacologic intercession for those with either eyebrow/scalp AA. In majority cases, regularly used preparation is triamcinolone acetonide (TA), at formulation of 2.5-10 mg/ml. TA is available as 40 mg/ml. Platelet-rich plasma (PRP) has become advanced technique for the management of various types of alopecia. It is an autologous formulation of higher platelet concentration having multiple growth factors.[8] These diverse factors have potential for advancing cell multiplication and separation due to which PRP has discovered numerous applications also in other fields like in Dentistry, Orthopedics, Dermatology and wound management.[9]

Rationale

As no local study is available and international data is not extensively available to draw any conclusion. This study can help us to generate evidence regarding role of PRP specifically in alopecia areata.

Operational Definition

Severity of Alopecia Tool (SALT): SALT calculation relies over scoring system.7 Scalp area is apportioned in four sections:

- Top: 40% (0.4) of surface area.
- Right half: 18% (0.18) of surface area.
- Left half: 18% (0.18) of surface area.
- Posterior: 24% (0.24) of surface area.

Portion of hair loss in these sections is the %age hair loss multiplied by % surface area of particular section. SALT score is calculated as total of percentage of hair loss in all sections described.

Efficacy: It was assessed in %age reduction in Severity of Alopecia Tool (SALT)

Material and Methods

The study design used in this study was Randomized controlled trial that was performed at Dermatology department, Lahore General Hospital, Lahore. The duration of study was 6 months from 6th July 2021 to 6th December 2021. Non-probability purposive sampling technique was used. Both genders with age group of 18-70 years were included. All patients diagnosed with AA and didn't take any medication for last 3 months were selected. All the patients having other type of alopecia, active local infection, atrophy of scalp because of previous treatment, taking any steroid or immunosuppressive drugs and history of any allergy or side effects were excluded from the study. Pregnant and lactating women were also excluded from the study.

A total of 180 cases meeting inclusion standards were recruited in study after getting approval from ethical committee of hospital. Patients were enrolled through OPD of Dermatology department of Lahore General Hospital. After a written informed consent, patient's contact information, demographic data and contact

details were obtained. Diagnosis of AA was confirmed in all cases depending over thorough clinical history (drugs related baldness), medical assessment and laboratory investigations. "Severity of Alopecia Tool" (SALT) score was used which relies over the concentration and magnitude of scalp baldness and evaluated through two investigators. Patients were randomly allocated into two groups:

All cases were randomized into 2 treatment groups randomly utilizing computer build random number table. TA (10 mg/ml) was intradermally received by Group-A, at the affected area and through a 0.5-inch long, 30-gauge needle in multiple 0.1ml injections around 1cm away from each other. PRP was given to Group-B that was made by utilizing double centrifugation method. About "20ml" blood was drained and centrifugation was performed at "5000rpm" for fifteen min. The red blood cells are segregated from plasma having platelets in the 1st spin. Afterwards, centrifugation was performed at "2000rpm" for 5-10 min on the remaining supernatent. This technique generated the required PRP. Lowest layer was obtained and an activator containing 10% $CaCl_2$ was mixed (0.3ml for 1ml of PRP). Dermapen was preferred for PRP application. Platelet-rich-plasma was made fresh for each session, and the remaining was not reused. Over-all three sessions were provided to every case at interim of 4 weeks, and a follow up at 3 months. During this time, no other treatment modality or management was used. A series of photos were taken and dermoscopic assessment was performed. Outcome was assessed based on the SALT score (as per operational definition). The patients were followed up at 4th, 8th and 12th weeks.

The data was analyzed through SPSS version 22. Descriptive statistics like age and score of Severity of Alopecia Tool was shown as mean ± standard deviation. Qualitative data such as gender, grades of improvement in alopecia areata was presented in from of frequency and %age. Independent sample t-test / Mann Whitney U test was used to contrast SALT score in both groups at each follow up visit. Chi-square test was used to match grades of improvement in both study groups. P-value ≤ 0.05 was considered as significant.

Table 1: *Descriptive Stats of Age in Both Groups*

	No. of cases	Mean	S.D	Minimum	Maximum
ITA	90	35.39	12.12	18	68
PRP	90	36.64	12.32	18	68
Total	180	36.02	12.20	18	68

ITA: Intralesional triamcinolone acetonide
PRP: Platelet rich plasma

Results

The mean age of patients with minimum and maximum age group is described in table 1.

In this study there were 109(60.56%) male and 71 (39.44%) female cases with 1.59:1 male to female ratio.

Table 2: *Comparison of Efficacy / Complete Resolution in both Groups*

		Groups		Total
		ITA	PRP	
Complete resolution	***Yes***	37(41.1%)	44(48.9%)	81(45%)
	No	53(58.9%)	46(51.1%)	99(55%)
Total		90(100.0%)	90(100.0%)	180(100.0%)

Chi-square = 1.10, p-value = 0.294

In ITA group there were 59(65.56%) male and 31 (34.44%) females and in PRP group there were 50 (55.56%) male and 40(44.44%) female cases.

The comparison of both groups with its complete resolution is mentioned in table 2

The complete resolution was statistically same in PRP group in comparison with ITA group, p-value = 0.294 i.e. > 0.05.

Discussion

Successful management of AA which can markedly modify the disease progression has been the topic of innumerable research trials in last many years. A lot of cases diagnosed with AA have not shown effective response towards routine medications and thus search for other therapeutic choices is still going on.[10] PRP is an autologous formulation of blood which is made by a platelet concentrating methodology. This regime was at first acquainted with the medicinal society when various researchers utilized it in the surgeries and furthermore in managing chronic non-healing wounds. From that point forward, this treatment has been utilized in different fields such as orthopedics, dental surgical procedures and aesthetic procedures because these platelets release various growth factors needed for healing.[11]

A placebo, double-blinded, and half head, comparative study was done in 45 cases to study efficacy of PRP among AA reasoned that it has no harm and is elective

cure of the disease. It considerably enhanced regrowth, decline dystrophy along with tingling perception deprived of much adverse effects.[12] Donovan presumed that PRP treatment could possibly manage AA (steroid resistant) comprising "ophiasis" and it can also be used as an alternative therapy in resistant cases constraining adverse reactions by steroid infusions.[13]

Similarly, another report deduced that individual managed by PRP had hair regrowth as initial reaction, decrease in short vellus hair and dystrophic hair comparable to cases managed with 5% minoxidil and control. The study reported the PRP therapy as increasingly compelling in managing AA as compared to 5% minoxidil.[14]

The use of steroids intralesionally are viewed as the essential pharmacologic intercession for those with either eyebrow and scalp alopecia and they can be carefully used by general doctors. The most regularly utilized agent is TA, at concentration of 2.5-10 mg/ml. It is commercially available as 40 mg/mL concentration and should subsequently be diluted in normal saline prior to use. Clinical response is seen in 2 -6 weeks. Abell and Munro effectively managed 71% of those with patch stage of AA utilizing intralesional steroids as first line management.[15]

PRP utilization was also assessed by another study conducted on half scalp, recruiting 45 cases (20 males, 25 females) randomized to get PRP therapy, 2.5mg/ml TA infusions, or placebo treatment. Despite the fact that the patients who were managed by either TA or PRP had altogether more noteworthy hair development contrasted with placebo treatment. Remarkably, cases managed by PRP indicated more noteworthy regrowth comparative with TA therapy. Also, rate of relapse by 12 month appeared to be increased in those managed with TA (71% versus 31%), proposing that PRP might be able to induce a prolong remission period. Strikingly, 96% cases managed by PRP seemed to regenerate hair pigment from the earliest starting point of regrowth compared with 25% cases managed by TA. These results favored the utilization of PRP to stimulate hair regeneration, particularly of colored hairs, along with low probability of recurrence.[16] PRP is generally safe procedure. Minor complications which have been observed include discomfort at administered site; mild pain, swelling, erythema, transient discoloration of skin and bruising.[17] The side effects observed during intralesional corticosteroid treatment are pain at injection site, telangiectasia, atrophy of skin, loss of pigmentation and cushingoid features because of systemic absorption. Transient atrophy is negligible that is usually seen due to infusion of high volume/infused site.[18] One study on alopecia areata depicted that the average age of the patient was 25.20 ± 11.11 yrs. Males comprised 79.2% of the study population. The male to female proportion was about 4:1.19 In this study the average age of patients was 36.02 ± 12.20 years. In this study there were 109 (60.56%) male and 71(39.44%) female cases with 1.59:1 male to female ratio. The mean age and gender distribution in our study was comparable with above cited study as we had higher mean age and male to female ratio was also different in our study.

In Intralesional TA group 37(41%) of patients had complete resolution while 53(58.9%) of the cases did not have complete resolution. In PRP group 44(48.9%) of the patients had complete resolution and 46(51.1%) of the patients did not have complete resolution. The complete resolution was statistically same in PRP group as compared to Intralesional TA group, p-value = 0.294 i.e. > 0.05. Study revealed that complete resolution percentage (53.8%) was greater in the PRP group in comparison with TA group (35.4%) toward the end of the 6th week, (p-value = 0.597). The general progress at ninth week and third month uncovered the fact that total regrowth of hair had been accomplished in all subjects of the two groups. Hence, PRP is a trouble-free, easy, economical and useful option in treating AA with efficacy equivalent to TA.[20] Similar to our study, a randomized, single-blinded, placebo and active-controlled comparative examination was done to compare the viability of intralesional PRP treatment with intralesional triamcinolone acetonide (ITA) in managing AA. They proposed that intralesional TA was found to give better outcome as compared to intralesional PRP. Subsequently it is inferred that Intralesional TA gives superior outcomes in AA than intralesional PRP.[20]

Compared with other modalities PRP is relatively harmless and possesses minimum adverse effects. Hence, PRP is a trouble-free, nontoxic, cost-effective and powerful modality for the management of AA with efficacy equivalent to triamcinolone.[21]

Conclusion

It is concluded that using PRP the frequency of complete resolution was higher than intralesional triamcinolone acetonide, but was not statistically significant. So, keeping in mind higher cure rate PRP injection can be used for treatment of AA as an easy, feasible and cost-effective management option.

Conflict of interest *None*

References

1. Naik PP, Farrukh SN. Association between alopecia areata and thyroid dysfunction. Postgraduate Med. 2021;133(8):895-8.
2. Salam S, Rafiq Z, Aziz N, Anwar A. Frequency of Alopecia Areata with other autoimmune disorders. The Professional Med J. 2022 ;29(02):227-31.
3. Sterkens A, Lambert J, Bervoets A. Alopecia areata: a review on diagnosis, immunological etiopathogenesis and treatment options. Clinic experiment Med. 2021; 21(2):215-30.
4. Deng W, Zhang Y, Wang W, Song A, Mukama O, Huang J, Han X, Deng S, Lin Z, Habimana JD, Huang R. Hair follicle-derived mesenchymal stem cells decrease alopecia areata mouse hair loss and reduce inflammation around the hair follicle. Stem Cell Research Therap. 2021;12(1):1-1.
5. Kouassi YI, Gbandama KK, Kourouma HS, Kouassi KA, Allou AS, Kaloga M, Ahogo KC, Kassi K, Kouame K, Ecra EJ, Gbery IP. Alopecia areata in Black African patients: epidemiological, clinical, and therapeutic aspects. Our Dermatology Online/Nasza Dermatologia Online. 2021;12(1).
6. Pratt CH, King LE, Messenger AG, Christiano AM, Sundberg JP. Alopecia areata. Nature reviews Disease primers. 2017 ;3(1):1-7.
7. Boyle FM, Shaw J, Young A, Hurk CV, Rugo HS, Fogarty GB, Lacouture ME. Management of alopecia due to cancer therapies. InThe MASCC textbook of cancer supportive care and survivorship 2018 (pp. 621-631). Springer, Cham.
8. Semsarzadeh N, Dover JS. PRP for Immune Mediated Alopecias (Alopecia Areata, Alopecia Totalis). InAesthetic Clinician's Guide to Platelet Rich Plasma 2021 (pp. 83-96). Springer, Cham.
9. Suruchi G, Shweta M, Chandi G. The wonder tool platelet rich plasma in cosmetic dermatology, trichology and hair transplant. In Dermatol Surg and Procedures 2018. IntechOpen.
10. Das A, Kumar P. Patchy Hair Loss. In Pediatric Autoimmunity and Transplantation 2020 (pp. 469-474). Springer, Cham.
11. Li S, Xing F, Luo R, Liu M. Clinical Effectiveness of Platelet-Rich Plasma for Long-Bone Delayed Union and Nonunion: A Systematic Review and Meta-Analysis. Frontiers in Medicine. 2021;8.
12. Gentile P, Cole JP, Cole MA, Garcovich S, Bielli A, Scioli MG, Orlandi A, Insalaco C, Cervelli V. Evaluation of not-activated and activated PRP in hair loss treatment: role of growth factor and cytokine concentrations obtained by different collection systems. Internation J molecul Sci. 2017 ;18(2):408.
13. Donovan J. Successful treatment of corticosteroid-resistant ophiasis-type alopecia areata (AA) with platelet-rich plasma (PRP). JAAD Case Reports. 2015 ; 1(5): 305-7.
14. El Taieb MA, Ibrahim H, Nada EA, Seif Al-Din M. Platelets rich plasma versus minoxidil 5% in treatment of alopecia areata: a trichoscopic evaluation. Dermatol therap. 2017 ;30(1):e12437.
15. Fathima S. Comparison of Various Treatment Modalities in patients with Alopecia Areata (Doctoral dissertation, Madras Medical College, Chennai). 2019
16. Hesseler MJ, Shyam N. Platelet-rich plasma and its utilities in alopecia: a systematic review. Dermatol Surg. 2020 ;46(1):93-102.
17. Almasri RA, Alomawi MA, Fahad M, Alhabshan HA, Alosaimi MS. Number of cosmetic procedures among women in Saudi community. Internation J Med in Developing Countries. 2019;3(11):920-5.
18. Alkhalifah A. Alopecia Areata. Practical Pediatric Dermatol. 2016:101-11.
19. Agrawal P, Jerajani HR, Jindal S. Intralesional platelet rich plasma therapy vs intralesional triamcinolone acetonide for the treatment of alopecia areata. MGM J Med Sci. 2018;5(2):68-75.
20. Fayed HA, Elsaied MA, Faraj MR. Evaluation of platelet-rich plasma in treatment of alopecia areata: a placebo-controlled study. J Egyptian Women's Dermatol Society. 2018 ;15(2):100-5.
21. Ranpariya RH, Gupta SB, Deora MS, Agrawal PV, Mathur R, Raheja A. Intralesional triamcinolone acetonide versus platelet rich plasma: a comparative study in the treatment of alopecia areata of scalp. Int J Res Dermatol. 2019 ;5(3):521-7.

Authors Contribution

AS: Conceptualization of Project
HF: Data Collection
ZS: Literature Search
A: Statistical Analysis
SS, UA: Drafting, Revision
HF: Writing of Manuscript

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