pISSN 1997-3438
eISSN 1997-3446
Indexed in
Index Pakistan (IP/016)
WHO Index Medicus (IMEMR)
EMBASE
EBSCO
Clavirate
IMEMR
Asian Digital Library (ADL)
Elsevier
Pakmedinet
NETMEDICS
ISI
Scopus
Recognized by
PM&DC
HEC
http://www.jmedsci.com

QUARTERLY

JOURNAL OF MEDICAL SCIENCES

PESHAWAR - PAKISTAN

Recognized by Higher Education Commission of Pakistan

J Med Sci 2022 July;30(3)

KHYBER MEDICAL COLLEGE, PESHAWAR - PAKISTAN

JOURNAL OF MEDICAL SCIENCES

Printed at:
Khyber Prints
E-mail: khyberprints@gmail.com

J Med Sci 2022 July;30(3)
http://www.jmedsci.com

Journal of Medical Sciences (Peshawar, Print/Online) is a peer reviewed open access journal that publishes biomedical public health and educational research on quarterly basis.

Editorial correspondence should be addressed to:

Associate Prof. Dr. Mohsin Shafi
Managing Editor JMS
Peshawar - Pakistan
E-mail: contact@jmedsci.com

CONTENTS

Journal of Medical Sciences is published on controlled circulation basis and distributed among the faculty of all national medical colleges, main libraries throughout the province, Pakistan Medical Research Council, PMDC, HEC and Tertiary Referral Centers.

The publisher and the members of the Editorial Board can not be held responsible for errors or for any consequences arising from the use of information contained in this journal.

Journal of Medical Sciences is published quarterly, composed and printed at Khyber Printers, Peshawar KP, Pakistan.

Annual Subscription
Pakistan: Rs. 5000/-
Overseas: US $ 500/-

Printed at:
Khyber Prints
E-mail: khyberprints@gmail.com

EDITORIAL

STUDENT SELECTED COMPONENTS: A WAY FORWARD TO SELF-DIRECTED INDEPENDENT LEARNING

Muhammad Naeem

Department of Surgery, Khyber Teaching Hospital, Peshawar - Pakistan

This editorial may be cited as: Naeem M. Student selected components: A way forward to self-directed independent learning. J Med Sci 2022 July;30(3):165-166

"You cannot teach people anything. You can only help them discover it within themselves" – Galileo Galilei

Recent advancements in the realm of medical education around the world have introduced major shifts in the traditional paradigm of learning and teaching. This has led to a transition from teacher-centered to student-centered learning, having an impact on both under and post-graduate medical students[1]. Student-selected components, previously called Special Study Modules are elective components in the undergraduate medical curriculum, initiated for the first time after the suggestions of the 2002 report, "Tomorrow's Doctors", by the General Medical Council (GMC), that the medical curriculum should comprise student preference[2]. It is for this reason, that the Department of Medical Education is planning to launch Student Selected Components in the years 4 and 5 of undergraduate medical education in the coming academic sessions.

Student-selected components (SSCs) are a novel approach to medical education. They are an integral part of the undergraduate medical curriculum and offer an option to medical students to select and study a topic of their interest in depth. Five common purposes of SSCs have been described in the literature that includes:

- to help all medical students lengthen the depth of their learning, and improve their experiences above those included in the core curriculum;
- to offer opportunities for in-depth learning to the students in fields of interest either outside or within the core curriculum;
- to enhance teamwork, communication skills, professionalism, and research skills among medical students;
- to offer distinctive opportunities for personalized professional development in future careers[3];
- to help promote self-directed learning and make undergraduate medical students independent learners

It is expected that in a standard 5 years undergraduate medical curriculum, 25% to 33% of time should be dedicated to Student Selected Components. The SSCs along with the core curriculum must allow students to achieve the learning outcomes. Even though SSCs have received global recognition in the development of undergraduate medical curricula, there seems a lack of consensus regarding learning objectives, outcomes, composition, and contribution to an overall assessment of medical graduates[4].

The Department of Medical Education at Khyber Medical College is planning to formulate and implement student-selected components in the upcoming academic year over a wide range of modules related to medical and surgical subspecialties, pharmacy, health research, community-based activities, social welfare, and humanities. The principal stakeholders comprise Dean KMC, the Director of Medical Education, the faculty members, the SSCs organizer and coordinator, administrative staff, regulatory bodies, and most importantly the students.

Certain challenges are expected during the process of launching this new program. These include a mutual consensus among the principal stakeholders including medical educationists, faculty members, and students regarding the selection of various modules. There might be problems related to the adjustment of SSCs modules in the timetable based on the mandatory core curriculum. There might be competition for certain modules among students and others might be altogether overlooked by students. The selection of students for certain highly rated modules like minimal access surgery or interventional radiology may be a problem due to tough competition among students. The unavailability of clinical rotations for certain subspecialties as desired by the medical students in the parent hospital might pose another problem. Lack of uniformity in the learning outcomes, mode of information transfer, skills achieved, standardization of assessment, and its contribution to the overall summative assessment are other challenges. In a developing country

like ours, resources management, training, and support of students and faculty to achieve the desired outcomes might be difficult. The mutual consensus among the principal stakeholders can be achieved through rounds of meetings, based on the rationale and need assessment for the SSCs. The need assessment can be performed through surveys among students and faculty members. The issue of management of SSCs in the timetable can be managed by planning for clinical rotations in summer vacations as SSCs are based on student preferences. The allocation of SSC modules should be based on the student's summative assessment in the previous year and module-related basic knowledge assessed through an MCQ/SEQ test. The unavailability of certain subspecialties in the parent hospital can be managed by collaboration with the stakeholders of the nearby tertiary care hospitals in the city. The lack of uniformity in the learning outcomes, mode of information transfer, skills achieved, and standardization of assessment can be managed by developing consensus among faculty members and supervisors of individual modules. Short refresher courses and symposia might prove helpful to narrow the wide gulf between resources management, training, and support of students and faculty members.

It is well said that when there is a will there is a way. All the above-mentioned challenges can be effectively managed through cooperation and trust, proper communication, and teamwork among the principal stakeholders. The feedback from the students and faculty members can be very helpful in the evaluation of the outcomes achieved through this program.

REFERENCES

1. Jawaid SA. Professionalism in Medical Journalism and Role of HEC, PM&DC. Annals of King Edward Medical University. 2016;22(3).
2. Christopher D, Harte K, George C. The implementation of Tomorrow's Doctors. Medical Education. 2002;36(3):282-8.
3. Murdoch-Eaton D, Ellershaw J, Garden A, Newble D, Perry M, Robinson L, et al. Student-selected components in the undergraduate medical curriculum: a multi-institutional consensus on purpose. Medical Teacher. 2004;26(1):33-8.
4. Riley SC, Ferrell WR, Gibbs TJ, Murphy MJ, Cairns W, Smith S. Twelve tips for developing and sustaining a program of student selected components. Med Teach. 2008;30(4):370-6.

Dr. Muhammad Naeem
Associate Professor
Department of Surgery,
Khyber Teaching Hospital, Peshawar - Pakistan
Email: muhammad.naeem@kmc.edu.pk
Cell: +92-314-9960600

ORIGINAL ARTICLE

EFFECTIVENESS OF DRAINLESS THYROIDECTOMY IN TERMS OF POSTOPERATIVE BLEEDING-A RANDOMIZED CONTROLLED TRIAL

Muhammad Naeem[1], Qaviullah Mian[1], Wajeeha Arshad[1], Mushtaq Ahmad[1], Yasir Hakim[2]

[1]Department of Surgery, Khyber Teaching Hospital, Peshawar - Pakistan

[2]Department of Surgery, Naseer Teaching Hospital, Peshawar - Pakistan

ABSTRACT

Objective: To determine the effectiveness of drainless thyroidectomy in terms of postoperative bleeding.

Material & Methods: This randomized controlled trial was conducted in Khyber Teaching Hospital on 40 patients from January 2019 to December 2019 after getting ethical approval from the hospital ethical committee. Two groups were allocated consisting of 20 patients, one with drainage and one without drainage, and were observed for bleeding during their stay in the hospital postoperatively. Data was collected using SPSS-21 to compare the effectiveness of both the procedures and the results were described in the form of tables.

Results: The difference in complication rates was not significant in the two groups. In the drainless group, two cases of seroma (5%) were noted in both groups. One case of hematoma was observed in the drain group. No case of hematoma was reported in the drainless group.

Conclusion: The use of drainless thyroidectomy can be justified based on the available data in this study where no bleeding was observed in the intervention group.

Keywords: Thyroidectomy, drains, post-operative complications

This article may be cited as: Naeem M, Mian Q, Arshad W, Ahmad M, Hakim Y. Effectiveness of drainless thyroidectomy in terms of postoperative bleeding-a randomized controlled trial. J Med Sci 2022 July;30(3):167-170

INTRODUCTION

Thyroidectomy, a commonly performed surgical procedure, has many possible complications if not performed by expert surgeons. A notable complication is a postoperative hemorrhage that may prove lethal by causing acute upper airway obstruction.[1]

In anticipation of a hematoma resulting in compression of the airway and respiratory distress, surgeons have conventionally used drains post-operatively. Many research reports provide no rationale for the use of drains however to prevent major bleeding, the majority of surgeons favor placing a drain.[2-4]

Most randomized clinical trials recommend drainage only in patients undergoing major thyroid surgeries like those with large goiters, thyroid carcinomas, any evidence of coagulopathy, or thyroidectomy with neck dissection. Benign thyroid diseases require less extensive operations and placing drains has not been proven to be productive.[1-3]

Most studies propose that the use of drains worsens patient discomfort, increases the rate of surgical site infections, and prolongs hospital stay thus increasing expenses, with unsatisfactory cosmetic results. Various randomized clinical trials have given little indication for the habitual use of drains after thyroid surgery.[5,6]

In contrast to this, a study suggests that even extensive thyroid surgeries can be performed without using drains safely and with the additional advantage of reducing hospital stay and eventual cost reduction for the patients. [7] Larger number of procedures which leave a huge dead space such as colorectal, plastic surgery, vascular, and orthopedics are now not frequently drained, thus raising doubts about the use of drains in thyroid surgeries.[8]

Previous reports also outline how a drain can play a role in initiating fluid formation rather than putting a stop to it owing to its foreign body property.[9] A European study showed that in terms of efficacy no hematoma was found in 99% of the drain group while 92% in the no drain group.[10]

The current study is aimed to find the effectiveness

Correspondence
Dr. Qaviullah Mian
Trainee Registrar
Department of Surgery, Khyber teaching hospital, Peshawar - Pakistan
Cell: +92-344-1969479
Email: kvkav19@gmail.com
Date Received: 27-01-2021
Date Revised: 20-09-2022
Date Accepted: 23-09-2022

of drain after thyroid surgery in our local population after comparing it with the non-drain group. The rationale behind doing this study is that there is a great need of developing local statistics in our population about the effectiveness of routine drainage after thyroidectomy.

MATERIAL AND METHODS

After informed written consent from patients and ethical approval from the ethical committee, we conducted this trial in Surgery Department, Khyber Teaching Hospital, from January 2019 to December 2019 on 40 patients with a 6 months follow-up. Patients befitting inclusion criteria presenting in OPD were recruited in the study which included either gender and age 18-60 with goiters needing surgery.

Detailed history followed by a thorough clinical examination was performed and appropriate investigations were ordered. The lottery method was used to allocate patients into two groups. Patients in whom drain was kept were allocated to group A and those in whom drain was not kept were allocated to group B. Surgical procedures were conducted as per general surgery protocols and were conducted by a surgeon having a minimum of 10 years of post-fellowship experience. Before wound closure, closed suction drains were placed in group A.Using SPSS version 21, the student t-test was used to find the differences between the two groups.

RESULTS

Among the 20 in the drained group, 7 were men and 13 women with a mean age of (43.8±9.3) years. On the other hand, 8 out of 20 in the non-drained group were men and the remaining 12 were women with a mean age of (45.1±11) years. The difference in gender distribution was reported to be non-significant between the two groups (P=0.42). The results are plotted in the tables below.

In the drainless group, 9 patients (45%) were discharged before 48 hours, half of the group (10 patients, 50%) were discharged on 3nd day while 5% (1 patient) were discharged 4th day. However, in the drained group, two patients were discharged before 48 hours while the rest of them were discharged on the 3rd day and 4th day. The mean stay for the drainless group was quite shorter as compared to the drained group (P=0.00005).

DISCUSSION

Throughout the world, surgeons rely on the use of drains routinely in thyroid surgery, not because of comprehensive evidence present, but rather owing to their own experience and customs.[11] The idea of placing a drain is the belief that it is going to suck out and evacuate the existing hematoma and the reactionary fluid collected, hence its role in preventing one of the disastrous complications of thyroid surgery and making surgeons watchful for any major bleed.[12] However, the use of a drain might be totally useless in straightforward easy cases owing to adequate hemostasis and perhaps the only salvage for prevention of hematoma formation which cannot be rightly replaced by a drain. Hence no guarantee of fluid/hematoma collection in drained patients.[13] Moreover, infections are amenable to the placement of drains.[14] The practices in thyroid surgeries had considerably improved over the past decade with a major decline in morbidity and mortality. Multiple complications which were grave enough to cause death including major bleeds, and hematoma formation leading to dyspnea and apnea have been cut down due to smart improvisation.[11] Such trends have put a question mark on the use of drain in thyroid surgery. So far, many trials failed to answer this question satisfactorily. While the majority of the surgeons are of the opinion that drainage might be completely unnecessary in thyroid surgery.[12]

Patients who underwent total thyroidectomy or lobectomy for benign thyroidal diseases were included in our study. Khanna et al demonstrated that in the drainless group, 4% of their patients developed seroma, 7% had hypoparathyroidism and no case was reported of wound infection and hematoma formation. In the drained group, 5% suffered seroma formation, 5% went through the suffering of wound infection, and 3% developed hy-

Table 1: Comparison of time, weight, VAS score, Amount of analgesia, and hospital stay between 2 groups.

Parameters		Drained	Non-Drained	P-Value
Operating Time (min)		146.10±28.16	131.20±29.09	0.52
Weight of Specimen (g)		224.88±232.85	220.21±205.27	0.72
VAS Score	POD 0	5.10±0.89	4.05±1.11	0.0014
	POD 1	2.45±1.01	1.75±0.69	0.0095
		47.05±12.4	28.40±13.85	0.00005

Table 2: Comparison of Post-operative complications between the 2 groups.

Complications	Drained (group A)	Non-Drained (group B)
Hematoma	0 (0%)	0 (0%)
Seroma	2 (5%)	2 (5%)

poparathyroidism with no hematoma formation.[12] Our study demonstrated similar results to that of Khanna et al. The complication rates were not significantly different in the two groups in our study. one case of seroma (5%) occurred in the non-drained group, whereas one case of seroma (5%), and 1 case of wound infections (5%) occurred in the drained group. No case of hematoma was reported in either group. Adequate and meticulous hemostasis is the cornerstone of such results.

There were no patients requiring a surgical revision or re-operation for the complications encountered. Successful management of all complications with palliative care was reported which is similar to the literature worldwide.[15-18]

Nevertheless, wound complications that likely occurred in the drained group in our study cannot be ignored, owing to the drain placement. Hence drains predispose wounds to the development of infections.[19] A study conducted by Schietroma et al. suggested that VAS was almost half in the drainless group which clearly points toward the association of pain with the placement of drains.[20]

Whether patients can be sent home depends not only on the collection at the wound site but also on their post-operative pain status, and their will of returning to daily life activities which are markedly influenced by their surgery satisfaction and ease. The study suggested that hematoma formation with respiratory symptoms occurs within the 1st 6 hours of surgery, hence routinely, patients must be observed on 1st postoperative day.[9] In the present study, no hematoma was formed in any of our groups.

This study is limited because a small number of patients are included. Also, a single-center study is a limitation too. Hence, a larger number with multiple center data would be required to enhance the results.

CONCLUSION

The use of drainless thyroidectomy can be justified based on the available data in this study. Moreover, collection in the form of seroma/hematoma cannot be prevented with drain if meticulous hemostasis is not achieved during surgery. Thus, drainless thyroidectomy is an option in patients undergoing the procedure.

REFERENCES

1. Edafe O, Cochrane E, Balasubramanian SP. Reoperation for bleeding after thyroid and parathyroid surgery: incidence, risk factors, prevention, and management. World journal of surgery. 2020 Apr;44(4):1156-62.
2. Panda NK, Sood M, Kaushal D, Bakshi J, Verma RK. How Long to Keep the Surgical Drains-Looking for Evidence. Journal of Otolaryngology-ENT Research. 2015;2(3):20-5.
3. Alamani JA, Reala ET, Castaneda SS, Chua AH. Drain verus No Drain After Thyroidectomy: A Preliminary Prospective Randomized Controlled Trial. PhiliPPine Journal of otolaryngology-head and neck Surgery. 2014 Jun 25;29(1):11-5.
4. Al-Habsi AS, Al-Sulaimani AA, Taqi KM, Al-Qadhi HA. Comparison of Postoperative Drain Insertion versus No Drain Insertion in Thyroidectomies: Retrospective case-control study from the Sultan Qaboos University Hospital, Muscat, Oman. Sultan Qaboos University Medical Journal. 2016 Nov;16(4):e464.
5. Li L, Chen H, Tao H, Liu W, Li W, Leng Z, Zhao E, Huang T. The effect of no drainage in patients who underwent thyroidectomy with neck dissection: A systematic review and meta-analysis. Medicine. 2017 Dec;96(50).
6. Kalemera SE, Fualal J, Jombwe J, Galukande M. To drain or not to drain after thyroid surgery: a randomized controlled trial at a tertiary Hospital in East Africa. African health sciences. 2013;13(3):748-55.
7. Suzuki S, Yasunaga H, Matsui H, Fushimi K, Saito Y, Yamasoba T. Factors associated with neck hematoma after thyroidectomy: a retrospective analysis using a Japanese inpatient database. Medicine. 2016 Feb;95(7).
8. Lee SW, Choi EC, Lee YM, Lee JY, Kim SC, Koh YW. Is lack of placement of drains after thyroidectomy with central neck dissection safe? A prospective, randomized study. The Laryngoscope. 2006 Sep;116(9):1632-5.
9. Hurtado-López LM, Zaldivar-Ramirez FR, Kuba EB, Cejudo AP, Flores JH, Solis OM, Castillo CC. Causes for early reintervention after thyroidectomy. Medical Science Monitor. 2002 Apr;8(4):CR247-50.
10. Portinari M, Carcoforo P. The application of drains in thyroid surgery. Gland surgery. 2017 Oct;6(5):563.
11. Colak T, Akca T, Turkmenoglu O, Canbaz H, Ustunsoy B, Kanik A, Aydin S. Drainage after total thyroidectomy or lobectomy for benign thyroidal disorders. Journal of Zhejiang University Science B. 2008 Apr 1;9(4):319-23.
12. Khanna J, Mohil RS, Bhatnagar D, Mittal MK, Sahoo M, Mehrotra M. Is the routine drainage after surgery for thyroid necessary?-A prospective randomized clinical study [ISRCTN63623153]. BMC surgery. 2005 Dec 1;5(1):11.
13. Maxwell J, Howe JR. Total Thyroidectomy. In: Operative Dictations in General and Vascular Surgery [Internet]. Cham: Springer International Publishing; 2017; 537–9
14. Salem FA, Almquist M, Nordenström E, Dahlberg J, Hessman O, Lundgren CI, Bergenfelz A. A Nested Case–Control Study on the Risk of Surgical Site Infection After Thyroid Surgery. World journal of surgery. 2018 Aug 1;42(8):2454-61.
15. Cannizzaro MA, Bianco SL, Picardo MC, Provenzano D, Buffone A. How to avoid and to manage post-operative complications in thyroid surgery. Updates in surgery. 2017 Jun 1;69(2):211-5.
16. Talukder DC, Sarker SC, Ahasan SA, Haque MM, Arefin MK, Musabbir N, et al. Evaluation of Post-operative Complications following Thyroid Surgery. J Dhaka Med Coll. 2020;27(2):108–13.
17. Eweida AM, Ebeed HM, Sakr MF, Hamza Y, Gabr E, Koraitim T, Al-Wagih HF, Abo-Elwafa W, Abdel-Aziz TE, Nabawi AS. Independent predisposing factors for subcutaneous and deep wound collection after total thyroid-

ectomy, a prospective cohort study. Annals of medicine and surgery. 2018 Dec 1;36:10-6.

18. Lang BH, Chan DT, Chow FC, Wong KP, Chang RY. The association of discolored parathyroid glands and hypoparathyroidism following total thyroidectomy. World journal of surgery. 2016 Jul 1;40(7):1611-7.

19. Emmi SM, Reddy MA. Thyroidectomy with and without drains: a clinical comparative study. International Surgery Journal. 2019 Apr 29;6(5):1584-8.

20. Schietroma M, Pessia B, Bianchi Z, De Vita F, Carlei F, Guadagni S, Amicucci G, Clementi M. Thyroid surgery: to drain or not to drain, that is the problem-a randomized clinical trial. ORL. 2017;79(4):202-11.

CONFLICT OF INTEREST: Authors declare no conflict of interest

GRANT SUPPORT AND FINANCIAL DISCLOSURE: NIL

AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under

Naeem M: Concept, design, data collection

Mian Q: Data collection, writing, review

Arshad W: Data collection, review

Ahmad M: Concept, review

Hakim Y: Concept, review

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

ORIGINAL ARTICLE

FACE WIDTH AS A VARIABLE INFLUENCING THE MESIODISTAL WIDTH OF PERMANENT MAXILLARY ANTERIOR TEETH: AN ANALYSIS USING AUTOCAD SOFTWARE

Momena Rashid[1], Shamayem Safdar[1], Faiza Ijaz[1], Sadia Hassan Khan[1], Syed Amjad Shah[2], Muhammad Sulaiman[3]

[1]Department of Oral Biology, Peshawar Rehman College of Dentistry, Peshawar - Pakistan

[2]Department of Oral and maxillofacial Surgery, Peshawar Dental College, Peshawar - Pakistan

[3]Department of Oral and maxillofacial surgery, Khyber College of Dentistry, Peshawar - Pakistan

ABSTRACT

Objective: The objective of this study was to determine face width as an important variable for the mesiodistal width of permanent maxillary anterior teeth in adult dentate subjects.

Material & Methods: It was an analytical cross-sectional study conducted in Oral diagnosis of Peshawar Dental College, Peshawar from February 2019 to April 2019.

A total of 180 subjects were included that fulfilled the inclusion criteria. Subject underwent the standard OPG procedure. JPEG file format of OPG images were analyzed by Autodesk AutoCAD software 2017 version to calculate the mesiodistal widths of permanent maxillary anterior teeth. Indirect mounting whipmix facebow model 9185 was used to measure face width by measuring the inter-condylar distance. The distance between two ear pieces of facebow was measured with the help of a digital caliper. One way ANOVA was run to see the effect in mesiodistal dimension of teeth widths among the three facial types.

Results: All the differences in mesiodistal widths of permanent maxillary anterior teeth among different facial widths were highly statistically significant (P<0.05).For all maxillary anterior teeth, the mesiodistal widths of teeth were larger in subjects with large facial width(148.05±1.61mm). In medium facial width (134.8±5.737mm) the teeth dimensions were smaller than large facial width but larger than in small facial width (118.75±2.647mm)

Conclusion: It was concluded that facial width had statistically significant association with the mesiodistal widths of permanent maxillary anterior teeth.

Keywords: Face Width, Maxillary Anterior Teeth, Autodesk AutoCAD Software

This article may be cited as: Rashid M, Safdar S, Ijaz F, Khan SH, Shah SA, Sulaiman M. Face width as a variable influencing the mesiodistal width of permanent maxillary anterior teeth: An analysis using AutoCAD software. J Med Sci 2022 July;30(3):171-175

NTRODUCTION

Dental esthetics is most dominant aspect of facial attractiveness and encompasses not only tooth colour, size and shape but also other aspects like upper lip position and gingival morphology.[1,2,3] Maxillary anterior teeth are considered the most dominant element in dental esthetics and facial esthetics because of amount of visible coronal structure.[4] Research has been carried out on determining the approximate width of maxillary anterior teeth by studying their relation with gender, race, facial profile, facial measurements and malocclusions. [5,6,7,8] This will help in providing data to dentists for, fabricating denture teeth in teeth selection for edentulous patients, orthodontic treatment planning ,restorative treatment.[9,10,11] In a study conducted in Lahore, Pakistan, a lower correlation between inter-condylar distance and maxillary inter-canine distance was found. There was a ratio of 3.7:1 between mean inter-condylar distance and mean inter canine distance of maxillary teeth.[12]

Another study in Iran studied the correlation between two facial widths (Bizygomatic width and inter-condylar width) and mesiodistal width of maxillary central incisors. It showed that there was a weak correlation between the inter-condylar width and right central incisor.[13]

In present study, the inter-condylar distance will

Correspondence
Dr. Momena Rashid
Senior Lecturer
Department of Oral Biology, Peshawar Rehman College of Dentistry, Peshawar - Pakistan
Cell: +92-333-9533076
Email: idrmominarasheed@gmail.com
Date Received: 27-01-2021
Date Revised: 20-09-2022
Date Accepted: 23-09-2022

be taken as a representative of facial width. Facial type or inter-condylar distance was measured with arbitrary facebow in these studies while in present study it will be measured with the help of indirect mounting whipmix facebow model 9185 which is an ear type of facebow with condylar rods that helps to measure intercondylar distance. Also, in these studies the mesiodistal widths of teeth were measured with help of Vernier calipers either directly on subjects teeth[10]or on dental casts while in this study mesiodistal width of individual teeth will be measured from the OPG images, with the help of Autodesk AutoCAD 2017 version software which is the latest version in AutoCAD series and best tool for this purpose.[7]

The aim of this study was to determine that face width is an important variable for the mesiodistal width of permanent maxillary anterior teeth in adult dentate subjects of age 15-25 years, using whipmix facebow.

MATERIAL & METHOD

It was an analytical cross-sectional study which was approved from ethical committee IRB/2020-257. Data was collected in Out Patient Department (OPD) of Peshawar Dental College from February 2019 to April 2019. By non-probability consecutive sampling technique, total of 180 subjects of both male and female gender were included, out of which 90 were males and 90 were females. Equal number of cases in small, medium, large face-widths were taken i.e. 60 small, 60 medium and 60 large face width cases. The age range was from 15-25 years. Informed consent was taken from all subjects. Exclusion criteria was subjects with missing permanent maxillary anterior teeth, anterior prosthesis or restorations, developmental anomaly of permanent maxillary anterior teeth, proximal surfaces alteration, history of orofacial surgery or orthodontic treatment. Inclusion criteria was subjects having fully erupted, structurally and periodontally sound maxillary anterior teeth that are having satisfactory alignment and with healthy Temporo-Mandibular Joint (TMJ).

Face width was calculated according to inter-condylar distance which is defined as the distance between each condyle as measured on the face of subjects from front view. It shall be calculated by a single examiner, using an indirect mounting whipmixfacebow model 9185 having a U-shaped frame. On anterior end, in front of anterior thumb screw it has marks to denote S(small), M(medium), L(large). The Thumbscrew was loosened, bitefork was positioned according to the midline, earpiece positioned in external auditory meatus, nose piece centered on nasion. The distance between the two earpieces of facebow shall be measured by using digital Vernier caliper having least count of 0.01mm.

Small width: Earpieces of facebow are <125 mm apart. Medium width: Earpieces of facebow are 125-145 mm apart. Large width: Earpieces of facebow are >145 mm apart.

Mesiodistal widths of permanent maxillary anterior teeth were calculated from OPG images of subjects which were imported to the drawing board of Autodesk AutoCAD software 2017 version. After selecting “millimeter” as a unit , the cursor was dragged from the most mesial point of the tooth to the most distal point of tooth and the measurement in information window was noted.

The data were entered & analyzed using computer program SPSS version 20.0. Frequencies and percentages were computed. Mean and standard deviation were calculated for all numerical variables like age and all maxillary anterior mesiodistal teeth widths. One-way ANOVA was run to compare maxillary anterior mesiodistal teeth widths among the three facial types. Post hoc analysis was done using Tucky test for multiple comparisons among various facial widths for mesiodistal teeth widths. $P<0.05$ was considered to be significant level.

RESULTS

Total 180 subjects were equally distributed in both genders. Gender distribution was equal i.e. n=90(50%) males and n=90(50%) females. The mean age was 22.19±2.57 (SD) years with a range of 15-25 years. The most common age group of the participants was 22 to 25 years with 116(64.44%) subjects followed by those having age group of 19-21 years that had 45(25%) subjects. Subjects in the age group 15-18 years were 19(10.56%). These details are graphically depicted in figure 1.

The mean mesiodistal width of right maxillary canine, lateral incisor and central incisor was 9.82±1.03 mm, 7.94±1.20 mm, and 9.47±1.43 mm respectively. The mean mesiodistal width of left maxillary canine, lateral incisor and central incisor was 9.82±1.08 mm, 8.03±1.10 mm, and 9.57±1.37 mm respectively. The detailed mean and standard deviation of age and maxillary anterior teeth is shown in table 1.

The mean facial width in small, medium and large facial type was 118.75±2.647, 134.8±5.737, 148.05±1.61 mm respectively. Their ranges are given in table 2.

Of total 180 subjects, there were equal number of cases in small, medium and large face width i.e. 60 small, 60 medium and 60 large face width cases. Irrespective of the maxillary anterior tooth, mesiodistal width was directly proportional to the width of the subject face. In medium facial width the teeth dimensions were smaller than those having large facial width but larger than those having small facial width. Mean maxillary right canine width was 9.32±0.84 mm, 9.77±0.9 mm and 10.4±1.08 mm in small, medium, large facial types respectively. Mean maxillary right lateral incisor width was 7.25±0.95 mm, 7.92±0.94 mm, and 8.64±1.28mm in small, medium, large facial types respectively. Mean maxillary right

central incisor width was 8.58± 1.02 mm, 9.37± 1.1 mm, and 10.5± 1.46 in subjects with small, medium, large facial widths respectively. Similar pattern was for left sided maxillary anterior teeth. All the differences in mesiodistal width of teeth among different facial widths were highly statistically significant (P<0.001). The details are shown in table 3.

Table 1: Mean and standard deviation for age and mesiodistal width of maxillary anterior teeth.

Variable	Range and Mean ± SD of all subjects	Mean ± SD	
		Male	Female
Age (years)	15-25, 22.19±2.57		
Right maxillary canine (mm)	7-13.3, 9.83±1.04	9.86± 0.95	9.79± 1.13
Right maxillary lateral incisor (mm)	5-11.7, 7.94±1.21	8.02± 1.08	7.85± 1.32
Right maxillary central incisor (mm)	6.3-14, 9.47±1.43	9.66± 1.29	9.28± 1.54
Left maxillary central incisor (mm)	6.4-13.7, 9.57±1.37	9.78± 1.19	9.39± 1.50
Left maxillary lateral incisor (mm)	5-11.2, 8.03±1.10	8.14± 0.98	7.92±1.21
Left maxillary canine(mm)	7-12.8, 9.82±1.08	9.89±0.96	9.74± 1.19

Table 2: Mean and standard deviation of different facial widths.

Face dimension	Mean ± SD(mm)	Range
Small (n=60)	118.75±2.65	112-124
Medium(n=60)	134.8±5.737	125-143
Large(n=60)	148.05±1.61	146-152

Table 3: Comparison of mesiodistal tooth width of maxillary anterior teeth among facial widths

Tooth	Face type	Mesiodistal widths of teeth	%95 CI**	P-value*
		Mean± SD(mm)		
Right maxillary canine	Small	0.84±9.32	(9.54 ,9.1)	<0.001
	Medium	0.9±9.77	(10.01 ,9.54)	
	Large	1.08±10.4	(10.67 ,10.1)	
Right maxillary lateral incisor	Small	0.95±7.25	(7.49 ,7.01)	<0.001
	Medium	0.94±7.92	(8.167 ,7.68)	
	Large	1.28±8.64	(8.97 ,8.31)	
Right maxillary central incisor	Small	1.02 ±8.58	(8.84 ,8.31)	<0.001
	Medium	1.1 ±9.37	(9.656 ,9.09)	
	Large	1.46 ±10.5	(10.84 ,10.1)	
Left maxillary central incisor	Small	0.96 ±8.74	(8.98 ,8.49)	<0.001
	Medium	1.12 ±9.49	(9.78 ,9.2)	
	Large	1.36 ±10.5	(10.88 ,10.2)	
Left maxillary lateral incisor	Small	0.97 ±7.37	(7.619 ,7.12)	<0.001
	Medium	0.96 ±8.1	(8.349 ,7.85)	
	Large	1.02 ±8.62	(8.885 ,8.36)	
Left maxillary canine	Small	0.92 ±9.29	(9.53 ,9.05)	<0.001
	Medium	0.99 ±9.72	(9.98 ,9.47)	
	Large	1.03 ±10.4	(10.7 ,10.2)	

*One-way ANOVA; significant level, P<0.05; **confidence interval

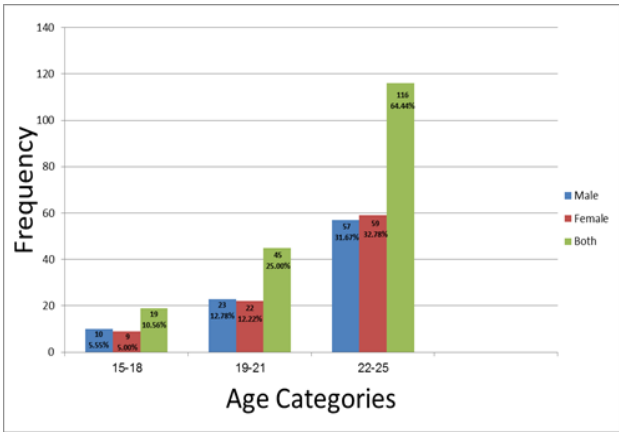

Fig 1: Age distribution of all subjects

DISCUSSION

This study determined if face width was an important variable for the mesiodistal widths of permanent maxillary anterior teeth in adult dentate subjects of age 15-25 years, visiting Out-patient Department of Peshawar Dental College in a 3 months' time interval, the measurements of teeth were done using soft images of subjects OPGs using Autodesk AutoCAD 2017 version software for measuring widths of teeth.

Tehranchi et al conducted a comparative study to measure mesiodistal widths of casts and reported AutoCAD software give a more precise result and manual method is only reliable when extreme caution is taken.[14] While previous studies used Vernier caliper and manual measurement which are less accurate and time consuming. These authors reported that Vernier caliper and manual measurement need extreme caution during calibration, duplicate measurements and averaging and also experience is a great factor for accurate measurement. [15-19] Thus, it implies that Autodesk AutoCAD software was considered as an appropriate tool for the measurement of mesiodistal widths of permanent maxillary anterior teeth.

For all maxillary anterior teeth, the mesiodistal widths of teeth were larger in subjects with large facial width(148.05±1.61mm). In medium facial width (134.8±5.737mm) the teeth dimensions were smaller than large facial width but larger than in small facial width (118.75±2.647mm) with P<0.05. (Table 3)

One of the most difficult aspects during the selection of maxillary anterior teeth for a removable prosthesis is the determining of appropriate mesiodistal width of six maxillary anterior teeth. Many attempts have been made to establish methods of estimating the combined width of these anterior teeth, and have to improve the esthetic outcome. The proportion of facial structures and relationship between facial measurements and natural teeth could be used as a guide in selecting denture teeth. There is a correlation between facial measurements and the mesiodistal width of the maxillary anterior teeth. According to Gomes et al the inter-canthal distance (r=0.466), inter-pupillary span (r=0.258), and inter-commissural distance (r=0.522) had a significant correlation to the mesiodistal width of the teeth. These results showed that as facial widths parameters are increasing the mesiodistal teeth width is also increasing. So large faces have larger teeth.[20]

Isa et al determined the relationships between some facial dimensions (inter- pupillary distance and inter-alar width) and widths of the maxillary anterior teeth to potentially provide a guide for tooth selection on 60 participants in Malaysia using regression methods.[21] Tripathi et al did correlation of inter-pupillary distance, inter-canthal width, bizygomatic width, and inter-alar width with inter-canine distance in Indian patients to determine the mesiodistal width of maxillary anterior teeth in edentulous patients. They found a statistically significant correlation (P<0.005) between these landmarks and the mesiodistal width of the maxillary anterior teeth.[22] These findings of all previous studies are supported by our findings.

Smith reported that nasal width, which is also considered as a type of facial width, had no significant correlation with width of six maxillary anterior teeth. There was a weak correlation in males(0.11) and females(0.23) and both were non-significant (P>0.05).[23] These results were not in accordance with this study.

On the basis of this study, it was observed that face width can be used for the purpose of selection of maxillary anterior teeth but it is not recommended to use it as a sole method for selection of maxillary anterior teeth; rather it should be used as a supplemental method. This is a single center, small sample and a hospital based study which may not represent Peshawar population. Further large sample and community based studies are recommended which will explore this area in depth.

CONCLUSION

According to this study, it is concluded that facial width had a statistically significant association with the mesiodistal widths of permanent maxillary anterior teeth, so these findings can be used as an appropriate guide for determining mesiodistal width for prosthetic maxillary anterior teeth in edentulous patients.

REFERENCES

1. McGowan S. Characteristics of Teeth: A Review of Size, Shape, Composition, and Appearance of Maxillary Anterior Teeth. Compen Continu Educat Dent.2016;37(3):164-171.
2. Chou JC, Thompson GA, Aggarwal HA, BosioJA, Irelan JP. Effect of occlusal vertical dimension on lip positions at smile. J Prosthet Dent.2014; 112(3):533-539.
3. Venugopal R, Ahmed A, Nichani A. Clinical assessment of the gingival contours and proximal contact areas in the maxillary anterior dentition. Gen Dent. 2017;

65(2):e7-e11.

4. Dalaie K, Behnaz M, Mirmohamadsadeghi H, Dashti M. Maxillary Anterior Teeth Width Proportion a Literature Review. EC Dent Sci. 2017; 16:197-206.
5. Fernandes TMF, Sathler R, Natalício GL, Henriques JF, Pinzan A. Comparison of mesiodistal tooth widths in Caucasian, African and Japanese individuals with Brazilian ancestry and normal occlusion. Dent Press J Orthod. 2013; 18(3):130-135.
6. Raghavendra N, Kamath VV, Satelur KP, Rajkumar K. Prediction of Facial Profile Based on Morphometric Measurements and Profile Characteristics of Permanent Maxillary Central Incisor Teeth. J Forensic Sci Med.2015; 1(1):26-32.
7. Mehndiratta A, Bembalagi M, Patil R. Evaluating the Association of Tooth Form of Maxillary Central Incisors with Face Shape Using AutoCAD Software: A Descriptive Study. J Prosthod. 2019; 28(2):e469-e472.
8. Malkoç S, Başçiftçi FA, Nur M, Çatalbaş B. Maxillary and mandibular mesiodistal tooth sizes among different malocclusions in a sample of the Turkish population. Eur J Orthod. 2010; 33(5):592-596.
9. Park DJ, Yang JH, Lee JB, Kim SH, Han JS. Esthetic improvement in the patient with one missing maxillary central incisor restored with porcelain laminate veneers. J Advanc Prosthod. 2010; 2(3):77-80.
10. Brandão RCB, Brandão LBC. Finishing procedures in Orthodontics: dental dimensions and proportions (microesthetics). Dent Press J Orthod. 2013; 18(5):147-174.
11. Frese C, Staehle HJ, Wolff D. The assessment of dentofacial esthetics in restorative dentistry: A review of the literature. J Am Dent Assoc. 2012; 143(5):461-466.
12. Shaikh IA, Qamar K, Naeem S. Relationship of the intercondylar distance with maxillary inter canine distance. Pak Oral Dent J. 2011; 31(2):470-473.
13. Jafari HJ, Radmehr O, Kaviani R, Valaei N. The analysis of correlation between the facial width and mesio-distal width of the maxillary anterior teeth. J Res Dent Sci. 2014; 11:49-53.
14. Tehranchi A, Nouri M, Massudi R, Katchooi M. Diagnostic value of manual and computerized methods of dental casts analysis. J Dent(Tehran). 2009; 6(2):85-90.
15. Asad S, Bokhari F, Ahsan W. Proportional mesio-distal dimension of permanent maxillary teeth. Pak Orthod J. 2015; 7(1):30-34.
16. Peckmann TR, LogarC, Garrido-Varas CE, Meek S, Pinto XT. Sex determination using the mesio-distal dimension of permanent maxillary incisors and canines in a modern Chilean population. Sci Justic. 2016; 56(2):84-89.
17. Rajat RK, Rishav S, Romil S, Nauseen H. Comparative evaluation of mesiodistal width of six maxillary anterior teeth in J&K population. Int J Sci Study. 2017; 5(7):4-7.
18. Sravya T, Dumpala RK, Venkateswara Rao Guttikonda PKM, Narasimha VC. Mesiodistal odontometrics as a distinguishing trait: a comparative preliminary study. J Forensic Dent Sci. 2016; 8(2):99-102.
19. Srivastava R, Jyoti B, Jha P, Gupta M, Devi P, Jayaram R. Gender determination from the mesiodistal dimension of permanent maxillary incisors and canines: An odontometric study. J Ind Acad Oral Med Radiol. 2014; 26(3):287-292.
20. Gomes VL, Gonçalves LC, Do Prado CJ, Junior IL, De Lima Lucas B. Correlation between facial measurements and the mesiodistal width of the maxillary anterior teeth. J Esthet Restor Dent. 2006; 18(4):196-205.
21. Isa ZM, Tawfiq OF, Noor NM, Shamsudheen MI, Rijal OM. Regression methods to investigate the relationship between facial measurements and widths of the maxillary anterior teeth. J Prosthet Dent. 2010; 103(3):182-188.
22. Tripathi S, Singh RD, Chand P, Kumar L, Singh GK. A study to correlate various facial landmarks with intercanine distance. Ind J DentRes. 2018; 29(4):440-444.
23. Smith B.J. The value of the nose width as an esthetic guide in prosthodontics. J Prosthet Dent. 1975;34(5):562-573.

CONFLICT OF INTEREST: Authors declare no conflict of interest

GRANT SUPPORT AND FINANCIAL DISCLOSURE: NIL

AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under

Rashid M:	Principal investigator, Concept and data analysis
Safdar S:	Data handling and critical analysis
Ijaz F:	Manuscript drafting
Khan SH:	Bibliography
Shah SA:	Proof reading and critical analysis
Sulaiman M:	Data entry

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

ORIGINAL ARTICLE

SOCIAL ISOLATION AND RESILIENCE COPING AS CORRELATES OF MENTAL ILLNESS IN ADULTS DURING COVID-19

Rabia Jameel[1], Sumbal Adeeb[1], Sara Latif[1], Mamoona Mushtaq[2], Shaista Jabeen[3]

[1]Riphah Institute of Clinical and Professional Psychology, Riphah international university, Lahore - Pakistan

[2]Department of Psychology, Government MAO College, Lahore - Pakistan

[3]Department of Psychology, Jinnah Hospital, Lahore - Pakistan

ABSTRACT

Objective: The current study has been designed to investigate the relationship between social isolation and mental illness and to identify the mediating role of resilience coping in adults.

Methods: The online data of 600 adults were recruited through a snowball sampling strategy. The age range of the participants was 18 years and above (M=25.64, SD=7.635). UCLA Loneliness Scale (Russel, 1996), Brief Resilience Coping Scale (Sinclair & Wallston, 2004), and Depression, Anxiety and Stress Scale (Lovibond & Lovibond, 1995) were used.

Results: Findings showed a significant positive association between social isolation and mental illness, while a negative association between social isolation and resilience coping. Additionally, resilience coping mediated the association between social isolation and mental illness [95% CI (LLCI: .0132, ULCI: .0802)].

Conclusion: Social isolation poses significant mental health risks and resilience coping can be used to improve mental illnesses.

KEYWORDS: COVID-19, Social Isolation, Resilience Coping, Depression, Anxiety, Stress, Mental illness.

This article may be cited as: Jameel R, Adeeb S, Mushtaq M, Jabeen S, Latif S. Social Isolation and Resilience Coping as Correlates of Mental Illness in Adults during COVID-19. J Med Sci 2022 July;30(3):176-180

INTRODUCTION

In early 2020, the entire world was gripped by the threat of developing a chronic infectious disease with the emergence of the menacing pandemic Corona Virus Disease, 2019 (COVID-19). Pakistan also faced this worldwide public health crisis. COVID-19 was and still is a global emergency with international concern requiring cooperation at the public level. Further, it requires safety measures to impede its rapid transmission rate and the substantial risk of contamination.[1] This led the health system globally to devise remedies to restrain the spread of disease and to have sound regulations in place.[2]

The most recommended and useful preventive strategy to control COVID-19 is social isolation.[3] In the context of COVID-19, social isolation is defined as physically separating oneself from others to avert the viral spread of a contagious disease.[4] It is a state of being alone i.e. avoiding the company of others and remaining in isolation from the community.[5] Social isolation also has been widely implemented in the past to impede or avoid the substantial transmission of viruses during pandemics such as Middle East Respiratory Syndrome, Spanish Flu, Ebola, and Plague.[6]

The Pakistani government initiated a nationwide lockdown and enforced curfews to hamper the community transmission of COVID-19. It was recommended during the lockdown in March 2020 to avoid social gatherings with more than 10 people. Social distancing measures suggest keeping a distance of at least 2m and avoiding unessential social activities. Stay-at-home orders were put in place and people were allowed to leave their houses only in case of emergency or for essential services.[7] These measures had prospective behavioral and clinical repercussions.[1] Restricting social interactions and isolating oneself physically could lead to boredom, lethargy, and exhaustion which could have a detrimental impact on health and can lead to chronic illness[8]. Social isolation results in a profound decrement in physical activity levels and is compounded by several mental problems such as stress, anxiety, and depression; frustration, adjustment disorder, post-traumatic stress disorder, and insomnia in people. [9, 10]

Individuals in social isolation experience intense

Correspondence
Dr. Rabia Jameel
lecturer
Riphah Institute of Clinical and Professional Psychology,
Riphah international university, Lahore - Pakistan
Cell: +92-323-4570729
Email: rabia.jameel@riphah.edu.pk
Date Received: 21-01-2021
Date Revised: 23-09-2022
Date Accepted: 24-09-2022

anxiety. They have irrational, illogical, and biased thoughts. The uncertainty associated with novel and comparatively acute infection increases the apprehension which gets amplified by isolation during the lockdown. People with other comorbidities are more vulnerable to these mental disorders as well as those working in the health care system such as doctors, nursing staff, and laboratories. Those who are quarantined for a long period are also vulnerable to developmental disorders.[11]

Individuals' coping style moderates the relationship between social isolation and mental health.[12] The individual employs various strategies to engage themselves and keep themselves busy or distracted.[13] Resilience coping – the tendency to cope with stress in a highly adaptive way, is a dynamic process comprised of positive adaptation in the face of severe adversity.[14] Resilience coping is associated with positive psychological as well as physical outcomes. Highly resilient individuals have more capacity to cope with social isolation without a mental breakdown. Resilient coping promotes the usage of adaptive cognitive and behavioral coping processes during the pandemic.[13]

In the context, mentioned above, the current study identifies the association of social isolation, resilience coping, and demographic variable (love for social gathering) with mental illness. Further, it investigates that resilience coping acts as a mediator between social isolation and mental illness (depression, anxiety, and stress).

MATERIAL & METHOD

Ethical clearance was obtained from the Ethical Review Committee (ERC) of Riphah Institute of Clinical and Professional Psychology (RICPP), Riphah International University, Lahore. Data was collected via an online survey from 7 major cities in the Punjab province of Pakistan. These were Lahore, Faisalabad Gujranwala, Rawalpindi, Sahiwal, Bahawalpur, and Sialkot. A total of 700 participants were approached via snowball sampling strategy and valid questionnaires were received back from 600 participants (358 women and 242 men; 85.71% response rate) aged 18 years and above (M=25.64, SD=7.635). An Online Google form was created, and all research protocols were uploaded on the form. Participants who followed the link arrived at the survey home page which contained the details of the study, minimal required age, institutional affiliations, and informed consent form outlining confidentiality and use of data only for research purposes as well as their right to withdraw from the research if they wanted to do so.

Participants who were not diagnosed with COVID-19, were at home for the last three months, not working, and were avoiding social gatherings and friends meet up were included in the research. Participants with COVID-19 positive, working from home, taking online classes, diagnosed with any mental disorder, diagnosed with severe physical illness, and participants looking after COVID-19 positive family member/s were excluded from the study. Moreover, participants who were bereaved by the death of a close family member within the past six months were also excluded.

Basic demographic details were obtained using a demographic questionnaire. It consisted of items related to age, gender, marital status, qualification, family system, residential area, religion, and profession of the participants. Further, it included items related to participants' sources of information about COVID-19 and their responses to it.

The UCLA Loneliness Scale was used to assess loneliness and social isolation among participants. It measures mild, moderate, and severe levels of loneliness. It is a 20 items self-reported measure with 4 points Likert scale ranging from 1 to 4 (1=never, and 4=always). The scale has high internal consistency ranging from 0.89 to 0.94.[15] Reliability for the current study was 0.84.

The Brief Resilience Coping Scale (BRCS) is a 4-item scale devised to measure coping tendencies with stress in a highly adaptive way. Respondents rate the items by using a 5-point Likert scale (1= does not describe me at all and 5= describes me very well). The internal consistency of the scale is 0.76[14] and the reliability for the current study was 0.71.

The Depression, Anxiety and Stress Scale (DASS-21) measures negative emotional states of depression, anxiety, and stress. The scale consists of 21 items, three sub-scales i.e. depression, anxiety, and stress, and responses are recorded on a 4-point Likert scale. Scoring ranges from 0 to 3 where 0 = never, Scale has excellent reliability 0.81 for depression, 0.89 for anxiety, and 0.78 for stress.[16] Internal consistency in the current study was good, 0.80 for depression, 0.86 for anxiety, and 0.75 for stress.

Data collected through the above-mentioned measures were analyzed statistically using SPSS-20. Descriptive and inferential statistics were used for analyzing the data. Inferential statistics included correlation and process analysis.

RESULTS

Total of 600 individuals 358 females (59.7%) and 242 males (40.3%) participated in the study. The age range of the participants was 18 years and above (M=25.64, SD=7.635). The majority 442 of the participants (73.7%) were unmarried. A large number of participants i.e., 372 (62.0%) came from the nuclear family system. The majority of the participants (i.e., 430; 71.7%) were educated until 14 years of education. Over fifty percent (N= 311,.51.8%) reported to get COVID-19 information from social media. Most of the subjects reported to be (424, 70.7%) were

afraid of COVID-19.

Table 1 indicates that individuals who have isolated themselves are more inclined towards mental illness and have less resilience coping. Furthermore, there was a significant negative association between love for social gatherings and mental illness indicating that an increase in social gatherings results in a decrease in mental illness. Moreover, there is a significant negative correlation between resilience coping and mental illness.

Table 2 demonstrates the association of mediator (resilience coping) with social isolation. PROCESS Analysis (Hayes, 2012) was used to examine the mediating role of resilience coping between social isolation and mental illness. The mediation model was tested in different steps. Path 'a' was tested in the first step by examining the association of social isolation (independent variable) with resilience coping (mediator). Findings concluded that social isolation significantly and negatively correlates with resilience coping, which points out that the increase in social isolation decreases resilience coping (b=-.057, p< .000) with a 0.02% variance.

In the second step path 'b' was tested and revealed a significant negative association between resilience coping (mediator) and mental illness (dependent variable). It was found that increase in resilience coping results in a decrease in mental illness. Findings showed that there was a significant indirect effect of social isolation on mental illness through resilience coping, the coefficient (social isolation and mental illness) was significant, B = .04, SE = .02, 95% CI = .0132, .0802.

Table 1: Descriptive Statistics and Correlation between Variables.

Variables	M	SD	1	2	3	4
1.Social Isolation	46.5	9.86	-			
2.Resilience Coping	13.8	3.34	-.16**	-		
3. Mental Illness	19.6	12.1	.43**	-.26**	-	
4. Love for Social Gathering	1.38	.48	.03	-.06	-.10**	-

Note: p< .01**, M= Mean, SD= Standard Deviation

Table 2: Association of Path 'a' (Independent Variable with Mediator)

Dependent Variable	Social Isolation (Independent Variable)		
	B	t (597)	P
Resilience Coping	-.05	-4.2	.00***

Note: p<.001***, t=test statistic, B=Unstandardized Coefficient.

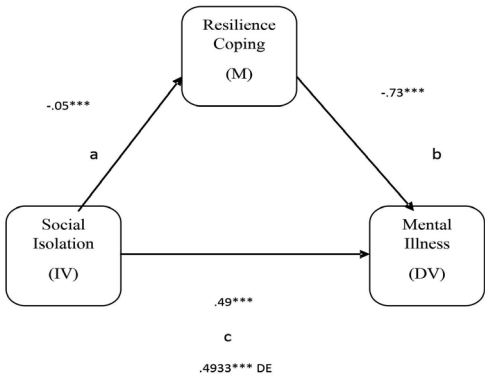

Fig 1: Showing results of the process when the hypothesis model was tested, with resilience coping as a mediator between social isolation and mental illness.

DISCUSSION

The findings of the current study established a clear linkage between social isolation and mental illness (depression, anxiety, and stress) during the COVID-19 pandemic. Social isolation has not only been found to be associated with cognitive decline and depression, but also it leads to physical deterioration. It negatively influences health via a complicated interconnected source.[17] Furthermore, isolation has a temporal and synergistic relationship with depression and it was identified as the distinguishing factor in predicting mental health problems in individuals.[12]

In the current study, a negative relationship emerged between social isolation and resilience coping. Social isolation is associated with maladaptive coping mechanisms and on contrary to it healthy socialization is linked with adaptive coping mechanisms.[12] Lonely and non-lonely adolescents both employ sad passivity and unhealthy coping styles. On the other hand, non-lonely youngsters adapt unhealthy coping styles only temporarily and prepare for more active coping styles. However, lonely adolescents employ maladaptive coping styles to a maladaptive degree.[18]

Findings indicate a positive relationship between the desire for social gatherings and mental health. These findings are in line with previous research confirming that socialization and healthy interaction with family members, relatives, colleagues, and friends reduce apprehensive, depressive feelings and result in developing feelings of security.[19] Likewise, another study revealed that individuals with a huge social circle, positive social relations, and support from significant others have the advantage of developing effective communication skills and reducing

depression and other mental health problems, and acting as a social cure for mental issues. [20,21] The current study found a positive relationship between fear of COVID-19 and mental illness. During a pandemic situation, fear increases cortisol levels and anxiety which makes the symptoms of mental disorders worse.[22, 23]

Lastly, it was found that resilience coping mediates the relationship between social isolation and mental illness. It was reported that coping is a strong negative predictor of depression and anxiety and is a significant predictor of mental health. [12,24] Previous research report positive and negative coping styles mediate the relationship between social isolation and adjustment.[13]

Implications of the study are manifold, including a guideline for mental health professionals to devise assessment procedures to identify the risk of developing mental illnesses during a pandemic or health crisis. Further, developing intervention strategies for those quarantined for long durations would be a cornerstone.

The data was collected online, hence there are some limitations, and the results should be interpreted accordingly e.g., the possibility of unreliable or fake responses and the unavailability of the researcher to answer the queries of the participants. Further, as data was collected from only major cities of Punjab, findings cannot be generalized to a larger population especially those from rural geographical vicinity.

CONCLUSION

Social isolation can have a drastic impact on the mental health of people. It can be a significant predictor of mental illness. Furthermore, resilience coping mediates the relationship between social isolation and mental illness.

REFERENCES

1. Pecanha T, Goessler KF, Roschel H, Gualano B. Social isolation during the COVID-19 pandemic can increase physical inactivity and the global burden of cardiovascular disease. Am J Physiol Heart Circ Physiol. 2020; 318(6): H1441-H1446. Doi: https://doi.org/10.1152/ajpheart.00268.2020
2. Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, et al. Early transmission dynamics in Wuhan, China, of novel Coronavirus infected pneumonia. N Engl J Med. 2020; 382(13):1199–207. Doi: 10.1056/NEJMoa2001316
3. World Health Organization. Coronavirus disease (COVID-19) advice for the public. World Health Organization, 2020. <https://www.who.int/emergencies/diseases/novel-coron avirus-2019/advice-for-public>.
4. Banerjee D, Rai M. Social isolation in Covid-19: The impact of loneliness. Int J Soc Psychiatr. 2020; 66 (6): 525-527. Doi: https://doi.org/10.1177/0020764020922269
5. Stickley A, Koyanagi A. Loneliness, common mental disorders and suicidal behavior: Findings from a general population survey. J Affect Disord. 2016; 197:81–87. Doi: 10.1016/j.jad.2016.02.054
6. Smith RD. Responding to global infectious disease outbreaks: Lessons from SARS on the role of risk perception, communication, and management. Soc Sci Med. 2006; 63(12):3113–3123. Doi: 10.1016/j.socscimed.2006.08.004
7. Raza A, 'Punjab govt's repeated pleas for social distancing fall on deaf ears', Geo News, Pakistan, 2020. March.
8. Chen Q, Liang M, Li Y, Guo J, Fei D, Wang L, et al. Mental health care for medical staff in China during the COVID-19 outbreak. Lancet Psychiatry.2020; 7(4): e15-e16. Doi: 10.1016/s2215-0366(20)30078-x
9. Banerjee D. The COVID-19 outbreak: Crucial role the psychiatrists can play. Asian J Psychiatr.2020; 50: 102014. Doi: 10.1016/j.ajp.2020.102014
10. Torales J, O'Higgins M, Castaldelli-Maia JM, Ventriglio A. The outbreak of COVID-19 coronavirus and its impact on global mental health. Int J Soc Psychiatry. 2020; 66(4):317-320. Doi: 10.1177/0020764020915212
11. Duan L, ZhuG. Psychological interventions for people affected by the COVID-19 epidemic. Lancet Psychiatry.2020; 7(4):300-302. Doi: 10.1016/s2215-0366(20)30073-0
12. Raut NB, Singh S, Subramanyam AA, Pinto C, Kamath RM, Shanker S. Study of loneliness, depression and coping mechanisms in elderly. J Geriatr Ment Health. 2014;1(1):20-27.Doi: 10.4103/2348-9995.141920
13. Quan L, Zhen R, Yao B, ZhouX.The effects of loneliness and coping styles on academic adjustment among college freshmen. Soc Behav Pers. 2014;42(6):969-977. Doi: 10.2224/sbp.2014.42.6.969
14. Sinclair VG, Wallston KA. The development and psychometric evaluation of the Brief Resilient Coping Scale. Assessment.2004; 11(1):94-101. Doi: 10.1177/1073191103258144
15. Russel DW. UCLA Loneliness Scale (Version 3): Reliability, Validity, and Factor Structure. J Pers Assess. 1996; 66(1):20-40. Doi: 10.1207/s15327752jpa6601_2
16. Lovibond SH, Lovibond PF.1995. Manual for the Depression Anxiety Stress Scales, Second ed. Sydney: Psychology Foundation. ISBN 7334-1423-0.
17. Bhatti AB, Haq AU. The pathophysiology of perceived social isolation: Effects on health and mortality. Cureus. 2017. Doi: 10.7759/cureus.994
18. Buskirk AMV, DukeMP. The relationship between coping style and loneliness in adolescents: Can "Sad Passivity" Be Adaptive? J Genet Psychol. 1991; 152(2):145-157. Doi: 10.1080/00221325.1991.9914662
19. Harandi TF, Taghinasab MM, Nayeri TD. The correlation of social support with mental health: A meta-analysis. Electron Physician. 2017; 9(9):5212–5222. Doi: 10.19082/5212

20. Marryam G, Sahar JS. The relationship between social support and mental health in Lorestan University students. Yafteh, 2010; 12(1):57–64.

21. Saeri AK, Cruwys T, Barlow FK, Stronge S, Sibley CG. Social connectedness improves public mental health: Investigating bidirectional relationships in the New Zealand attitudes and values survey. Aust N Z J Psychiatry. 2017; 52(4):365-374. Doi: 10.1177/0004867417723990

22. Shigemura J, Ursano RJ, Morganstein JC, Kurosawa M, Benedek DM. Public responses to the novel 2019 coronavirus (2019-nCoV) in Japan: Mental health consequences and target populations. Psychiatry Clin Neurosci. 2020;74(4):281-282. Doi: 10.1111/pcn.12988

23. Shultz JM, Cooper JL, Baingana F, Oquendo MA, Espinel Z, Althouse BM, et al. The role of fear-related behaviors in the 2013-2016 West Africa ebola virus disease outbreak. Curr Psychiatry Rep. 2016;18(11). Doi: 10.1007/s11920-016-0741-y

24. Felsten G. Gender and coping: Use of distinct strategies and associations with stress and depression. Anxiety Stress Coping. 1998; 11(4):289-309. Doi: 10.1080/10615809808248316

CONFLICT OF INTEREST: Authors declare no conflict of interest

GRANT SUPPORT AND FINANCIAL DISCLOSURE: NIL

AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under

Jameel R: Conceptualized the idea of this research. Prepared and edited the manuscript

Adeeb S: Conceptualized the idea of this research. Prepared and edited the manuscript

Mushtaq M: Conceptualized the idea of this research. Prepared edited and final review of the manuscript

Jabeen S: Conceptualized the idea of this research. statistical analysis and interpretation for the work.

Latif S: Prepared and edited the manuscript. Drafting the work or revising it critically for important intellectual content.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

ORIGINAL ARTICLE

DETERMINATION OF IMMUNIZATION STATUS AND ITS INVOLVED CHALLENGES AMONG HOSPITALIZED CHILDREN

Rahida Karim[1], Jahanzeb Khan Afridi[1], Akhtar Ali[2], Rizwanullah Jan[3], Muhammad Batoor Zaman[4], Afnan Amjad[5]

[1]Department of Paediatrics, Hayat Abad Medical Complex, Peshawar - Pakistan

[2]Category C hospital, Laki Marwat, KP - Pakistan

[3]Paediatric Cardiology, Children Hospital, University of Health Sciences, Lahore - Pakistan

[4]Department of Surgery, Khyber Teaching Hospital, Peshawar - Pakistan

[5]Department of Anaesthesia, Lady Reading Hospital, Peshawar - Pakistan

ABSTRACT

OBJECTIVE: To determine the immunization status and its involved challenges among hospitalized children.

Material and Methods: This cross-sectional study was conducted in the pediatrics department of Hayatabad Medical Complex Peshawar from February 2017 to September 2017. All children less than 5 years admitted via the outpatient department were included in the study. Their guardians were explained the purpose of the study and informed consent was obtained. A complete medical record of each individual including name, age, gender, detailed history, and examination was recorded in a predesigned Proforma. It also included details of immunization (fully immunized, partially immunized, or not immunized at all), Parental education (less than Primary and above Primary), socioeconomic status (poor, middle, and upper middle), and residential status (urban/rural).

Results: A total of 497 children were included in the study, out of which 422 were males (85%). A total of 419 (84.30%) were completely immunized, 65 (13.07%) were partially immunized and only 13 (02.61%) were not immunized. Among 84.30% of children who were completely immunized, their parents had an education status above primary schools. Thirty-six percent of fully immunized children belonged to poor socioeconomic status. Two third of the participants belonged to an urban community.

Conclusions: Ninety-seven percent of study participants were found to be completely/partially immunized. Most of the parents of immunized children had education status beyond primary school and were of upper and middle socioeconomic background. Most of them belonged to urban areas of the province.

Keywords: complete Immunization, partial immunization, Vaccination.

This article may be cited as: Karim R, Afridi JK, Ali A, Jan R, Zaman MB, Amjad A. Determination of Immunization Status and its Involved Challenges among Hospitalized children. J Med Sci 2022 July;30(3):181-184

INTRODUCTION

Vaccines have brought a revolution in the twentieth century by decreasing the morbidity and mortality due to infectious diseases and have improved life expectancy [1,2]. The EPI program was launched in Pakistan in 1978 to avoid vaccine-preventable deaths and illnesses (tuberculosis, diphtheria, pertussis, tetanus, polio, and measles). [3] Later on, it was extended and further vaccines were also added to the schedule against (Hepatitis B, H. Influenza, Pneumococcus, and Rotavirus). The targets were to eradicate polio by 2000, measles, and tetanus by 2015. [4-6] Unfortunately national immunization program coverage has increased but is consistently low. [7]

Our country ranks third in the world with unimmunized children and second in South Asia. Vaccine-preventable diseases account for 2-3 million deaths globally each year. [8] Fifteen percent of Pakistan's population is under 5 years and contributes to 50% of mortality. The death rate in children under 5 years is 8% worldwide. [9] Pakistan and Afghanistan have been unable to eradicate polio. [10] Therefore, efforts should be made to analyze the hurdles faced by Pakistan for the failure of adequate immunization.

Low immunization status in Pakistan has been linked to parental poverty, the father's profession, large family size, mothers' ignorance about health facilities, and the absence of antenatal care. [11, 12] Tetanus is the second leading cause of death in Pakistani infants (21.6%). [13] People have vaccine hesitancy due to misconceptions that it

Correspondence
Dr. Jehanzeb Khan Afridi,
Associate professor
Department of Pediatrics, Hayat Abad Medical Complex, Peshawar - Pakistan
Cell: +92-346-9090107
Email: zarakbehram@yahoo.com
Date Received: 23-12-2021
Date Revised: 21-09-2022
Date Accepted: 25-09-2022

may harm or sterilize their child. [14] Pakistan's 70% population belongs to rural areas and the vaccination profile is lower than urban. [11, 15]

Lower immunization status among the rural population may be due to difficulty in access to health care and utilization of services. If the vaccination center is within the range of 7 km, children are more likely to be vaccinated but if the distance increases, the chances of vaccination decline.[16]

The current study is conducted to determine the immunization status and its involved challenges among hospitalized children belonging to urban/rural areas around Peshawar. The results will help healthcare providers and policymakers address the issues identified.

MATERIALS AND METHODS

This cross-sectional study was conducted in the pediatrics department of Hayatabad medical complex Peshawar, Pakistan which is a 1200 beds tertiary care hospital in Peshawar, from February 2017 to September 2017. All children, of either gender, between 1 to 5 years admitted via outpatient department were included in the study. Their Parents/guardians were explained the purpose of the study and informed consent was obtained.

A complete medical record of each individual including name, age, gender, detailed history, and examination was recorded in predesigned Proforma. It also included details of immunization (fully immunized, partially immunized, or not immunized at all), Parental education (less than Primary and above Primary), socioeconomic status (poor, middle, and upper middle), and residential status (urban/rural).

A sample size of 497 was determined using the WHO sample size estimation software. The sampling was done through a non-probability consecutive sampling technique.

After the approval of the hospital ethical and research committee, data collection was started in the pediatrics unit. The collected data were analyzed in SPSS version 20 for windows. Percentages and chi-square test were calculated for categorical variables Immunization status was stratified among gender, parental education, and socioeconomic status to see the impact of modifications. All results are presented in the form of tables.

RESULTS

A total of 497 children were included in the study, out of which 42.4% of children were 1 to 2 years of age while 422 were males (85%) and the rest were females (table 1 and 2). A total of 419 (84.30%) were completely immunized, 65 (13.07%) were partially immunized and only 13 (02.61%) were not immunized. Among 84.30% of children who were completely immunized, 73.8% of parents had education status above primary schools (table 3). Thirty-six percent of fully immunized children belong to poor socioeconomic status (table 4). Two-thirds of the participants belonged to the urban community.

The age-wise distribution of groups showed that the 1 to 2 Years age group participants were 211 (representing 42.45% of the sample), while 3 to 5 age group participants were 286 (representing 57.54% of the sample). As per frequencies and percentages for immunization status, 419 (84.30%) patients were completely immunized, 65 (13.07%) patients were partially immunized and only 13 (02.61%) patients were not immunized at all. However, with respect to age, the future immunization status of the country is presenting a much more promising prospect, as projected in the figures of this study (table-1).

The education level was categorized in two levels; the one who has done at least primary education is being categorized as educated, while the other below primary is defined as uneducated in our study. Immunization status was high in children whose parents were educated (table no. 3).

Table 1: Stratification of immunization status with age.

Age	Immunization Status	Frequencies	Percentages
1 to 2 Years	Completely Immunized	179	36.01%
	Partially Immunized	28	5.63%
	Not Immunized at all	04	0.80%
3 to 5 Years	Completely Immunized	240	48.28%
	Partially Immunized	37	7.44%
	Not Immunized at all	09	1.8%

Table 2: Gender based stratification of immunization status.

Gender	Completely Immunized	Partially Immunized	No Immunization	Total
Male	360 (72.43%)	51 (10.26%)	11 (2.21%)	422 (84.9%)
Female	59 (11.87%)	14 (2.81%)	2 (0.40%)	75 (15.09%)
Total	419 (84.3%)	65 (13.07%)	13 (2.6%)	497

Table 3: Parental education and immunization status of children.

Status Education	Completely Immunized	Partially Immunized	No Immunization	Total
Above primary	367 (73.8%)	10 (2.01%)	2 (0.40%)	379 (76.25%)
uneducated	52 (10.466%)	55 (11.06%)	11 (2.21%)	118 (23.74%)
Total	419 (84.3%)	65 (13.07%)	13 (2.61%)	497

Table 4: Socioeconomic status and immunization status.

Socioeconomic status	Completely Immunized	Partially Immunized	No Immunization	Total
Poor	179 (36.01%)	48 (9.65%)	8 (1.60%)	235 (47.28%)
Middle	188 (37.82%)	12 (2.41%)	3 (0.60%)	203 (40.8%)
Upper middle	52 (10.46%)	5 (1.006%)	2 (0.40%)	59 (11.87%)
Total	419 (84.3%)	65 (13.07%)	13 (0.02%)	497

DISCUSSION

Immunization status reflects the success/failure of the immunization program in any country. Research has shown a lot of discrepancies in vaccine coverage in different areas of Pakistan. Trends vary in different provinces, in Punjab overall immunization coverage was 49% at the start, 66% in 2003, and 84% in 2005 but declined to 53%. Sindh followed the same trend. Sixty Percent of Balochistan's population had their vaccination in 1995 but later on, dropped to 35% by 2007 [7]. Complete immunization of 71.7% was reported from nine union councils of sub-district Gambat, Khairpur, and Sindh Immunization rate of 44.8% was recorded in a study conducted in a peri-urban area of Karachi. Studies conducted in the Faisalabad and Nurpur Shahan areas of Punjab revealed immunization coverage of 63% and 77.4%. [17] Overall efforts for immunization implementation have increased the coverage rate from 5 to84% [9]. A vaccination coverage rate of 59 to73% for all routine vaccines has been observed among 1 to 2 years old children, comparable to the current study. [18]

Gender discrimination is common in Asian countries, it is obvious in our study while another research (demographic and health survey 2006 -07) did not reveal a significant difference among partially vaccinated children male: female (64%:68%) and completely vaccinated 36%:31.4%.[19]

A lower parental educational level results in a lower level of understanding of the vaccination benefits and can be a target for myths (vaccination can sterilize /harm the child). A study conducted in Khyber Pakhtunkhwa Bannu District revealed a parental vaccination refusal rate of 27.9%, 79.3% of mothers and 65.9% of fathers were unable to read or write while in our study parental education rate above primary was 76.25% and may be the reason for the majority of children being completely vaccinated. In the same study, higher social class was linked to a higher vaccination refusal rate in contrast to our study where the majority of children from middle and high-income groups were vaccinated[12].

Seventy percent of Pakistan's population is from some rural areas and has lower vaccination coverage. The reason is poverty, ignorance, lack of knowledge about vaccines, misconceptions as well as failure to reach health services, as the distance increases beyond 7 km becomes difficult to avail .[16]

The current study, although, has localized population statistics can still be a guide for healthcare providers and policymakers to streamline the process of childhood immunization strategies.

CONCLUSION

Ninety-seven percent of study participants were found to be completely/partially immunized. Most of the parents of immunized children had education status beyond primary school and were of middle and upper socioeconomic background but belonged to urban areas of the province

REFERENCES

1. Greenwood B. The contribution of vaccination to global health: past, present, and future. Philosophical Transactions of the Royal Society B: Biological Sciences. 2014 Jun 19;369(1645):20130433.
2. Rappuoli R, Santoni A, Mantovani A. Vaccines: an achievement of civilization, a human right, our health insurance for the future. Journal of Experimental Medicine. 2019 Jan 7;216(1):7-9.
3. World Health Organization. Immunization coverage–fact sheet no. 378. World Health Organization. 2015
4. Ali SZ. Health for all in Pakistan: achievements, strategies and challenges. EMHJ-Eastern Mediterranean Health Journal, 6 (4), 832-837, 2000. 2000.
5. Closser S. "We can't give up now": global health optimism and polio eradication in Pakistan. Medical Anthropology. 2012 Sep 1;31(5):385-403.
6. Baloch MN, Siddiqui NZ, Bano A, Siddiqui S, Kiran T, Khan MK, Asad W. A cross sectional survey: Attitude towards adult vaccination in Karachi-Pakistan. International Journal of Advanced Research. 2015;3(3):512-2.

7. Hasan Q, Bosan AH, Bile KM. A review of EPI progress in Pakistan towards achieving coverage targets: present situation and the way forward. EMHJ-Eastern Mediterranean Health Journal, 16 (Supp.), 31-38, 2010. 2010.

8. Saeed R, Hashmi I. Pakistan Ranks Third Globally With the Most Unvaccinated Children: Is the Impact of Parental Perception and Attitude on Immunization an Essential Contributing Factor to an Unsuccessful Vaccination Coverage?. Cureus. 2021 Nov 19;13(11).

9. 9. Mansuri G, Rao V. Community-based and-driven development: A critical review. The World Bank Research Observer. 2004 Mar 1;19(1):1-39.

10. Verma AA, Jimenez MP, Tangermann RH, Subramanian SV, Razak F. Insecurity, polio vaccination rates, and polio incidence in northwest Pakistan. Proceedings of the National Academy of Sciences. 2018 Feb 13;115(7):1593-8.

11. Butt M, Mohammed R, Butt E, Butt S, Xiang J. Why have immunization efforts in Pakistan failed to achieve global standards of vaccination uptake and infectious disease control?. Risk management and healthcare policy. 2020;13:111.

12. Khattak FA, Rehman K, Shahzad M, Arif N, Ullah N, Kibria Z, Arshad M, Afaq S, Ibrahimzai AK, ul Haq Z. Prevalence of Parental refusal rate and its associated factors in routine immunization by using WHO Vaccine Hesitancy tool: A Cross sectional study at district Bannu, KP, Pakistan. International Journal of Infectious Diseases. 2021 Mar 1;104:117-24.

13. Siddiqi FJ, Rabbani F, Hasan R, Nizami SQ, Bhutta ZA. Typhoid fever in children: some epidemiological consideration from Karachi, Pakistan. Int J Infect Dis. 2006;10(3):215-22.

14. Hussain SF, Boyle P, Patel P, Sullivan R. Eradicating polio in Pakistan: an analysis of the challenges and solutions to this security and health issue. Globalization and health. 2016 Dec;12(1):1-9.

15. Mahmud G, Zaman F, Jafarey S, Khan RL, Sohail R, Fatima S. Achieving millennium development goals 4 and 5 in Pakistan. BJOG: An International Journal of Obstetrics & Gynaecology. 2011 Sep;118:69-77.

16. Naeem M, Adil M, Abbas SH, Khan MZ, Naz SM, Khan A, Khan MU. Coverage and causes of missed oral polio vaccine in urban and rural areas of Peshawar. Journal of Ayub Medical College Abbottabad. 2011 Dec 1;23(4):98-102.

17. 17. Rasheed M, Akram U, Asif N, Ahmed K, Zafar S, Mumtaz S. Expanded Programme of Immunization (EPI) status among children of factory workers. JIsb Med Dental Coll. 2014;2:62

18. 18. Okubo N, Matsuzaka M, Takahashi I, Sawada K, Sato S, Akimoto N, Umeda T, Nakaji S. Relationship between self-reported sleep quality and metabolic syndrome in general population. BMC public health. 2014 Dec;14(1):1-7.

19. Bugvi AS, Rahat R, Zakar R, Zakar MZ, Fischer F, Nasrullah M, Manawar R. Factors associated with non-utilization of child immunization in Pakistan: evidence from the Demographic and Health Survey 2006-07. BMC public health. 2014 Dec;14(1):1-7.

CONFLICT OF INTEREST: Authors declare no conflict of interest

GRANT SUPPORT AND FINANCIAL DISCLOSURE: NIL

AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under

Karim R: Concept, proposal, review

Afridi JK: Data collection, writing, review

Ali A: Writing, review

Jan R: Review

Zaman MB: Writing, review

Amjad A: Writing, review

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

ORIGINAL ARTICLE

FREQUENCY AND ANTIMICROBIAL RESISTANCE PROFILE OF SALMONELLA TYPHI ISOLATED FROM DISTRICT BUNER

Aftab Ali[1], Noor Rahman[1], Humera Adeeb[2], Ihsan Ullah[1]

[1]Department of Microbiology, Institute of Pathology and Diagnostic Medicine, Khyber Medical University, Peshawar - Pakistan

[2]Department of Community Medicine, Khyber Medical College, Peshawar - Pakistan

ABSTRACT

Objective: The objective of this study was to investigate the frequency and drug resistance of Salmonella typhi in district Buner, Khyber Pakhtunkhwa.

Material & Methods: This cross-section study was conducted at District Head Quarter Hospital Buner and private diagnostic centers from Jan 2020 to May 2021. A total of 460 blood samples were collected from OPD patients reported with signs and symptoms of Typhoid fever. Samples were cultured on blood and MacConkey agar, incubated at 37^{O} for 24 hours. Bacterial identification was done on colony morphology, gram staining, and polyvalent antisera for strain identification. Finally, antibiotic susceptibility testing was done for the isolated bacteria. All commonly prescribed first-line and second option antibiotics were tested on Mueller Hinton agar by Kirby Bauer disk diffusion method following CLSI guidelines 2020.

Result: A total of 240 out of 460 samples showed bacterial growth where Salmonella typhi was found in 98 (40.8%) cases. Among them, 28(28.6%) were reported as MDR while 1 (17.4%) were XDR. Out of the XDR, 4 strains were found resistant to Vancomycin and clarithromycin as well. The isolated S. typhi was 100% sensitive to Meropenem, and Azithromycin, however showed 100% resistance to Aztreonam, Ampicillin, and Cotrimoxazole. Prevalence of S. typhi was more (50%) in females while resistance was reported more in age group 20-40 years.

Conclusion: The frequency of Salmonella typhi at district Buner was 41% in patients reported with high grade fever where 28% of the strains reported were multidrug resistant. Some extended spectrum drug-resistant S. typhi and Vancomycin and Clarithromycin resistant strains were also reported which is alarming. Meropenem, and Azithromycin were the only drugs effective against most of the strains. However, resistance to these drugs may develop soon if we do not stop empirical excessive use of antibiotics.

Keywords: Multidrug resistant, Salmonella typhi, Typhoid fever, Extended spectrum drug-resistant

This article may be cited as: Ali A, Rahman N, Adeeb H, Ullah I. Frequency and antimicrobial resistance profile of Salmonella Typhi isolated from District Buner. J Med Sci 2022 July;30(3):185-189

INTRODUCTION

Enteric fever is caused by gram-negative bacteria, Salmonella enterica serovar typhi, and paratyphi. The disease is transmitted primarily by fecal-oral route predominantly via contaminated water and food [1, 2]. Typhoid fever is an acute febrile illness characterized by headache, nausea, anorexia, vomiting, constipation, and sometimes diarrhea [2, 3]. Mortality due to typhoid ranges from 1% to 3%, while global morbidity and mortality is reported more than 27 million per year and 200,000 per year respectively [4]. S. typhi infection is more common in South America, Asia, and Africa. According to a recent research, the prevalence of typhoid fever in India is 493.5/100,000 followed by Pakistan 412.5, Indonesia 180.3, Vietnam 24.4 and china 29.3 [4, 5].

Antibacterial drugs are recommended for the treatment of enteric fever worldwide. Unfortunately antibiotics resistance of Salmonella typhi has increased significantly during the last decade [1, 6]. Initially, the first-line anti-salmonella drugs were considered highly effective for the eradication of enteric fever which includes Ampicillin, Chloramphenicol, and Co-trimoxazole. However with the emergent of MDR, S. typhi in 1980, the first line drugs became useless and the pathogen developed resistance to all the three antibiotics. Thus treatment options changed to quinolones which was considered highly effective and fluoroquinolones became the drug of choice for salmonellosis. Unfortunately, resistance against fluoroquinolone developed soon which was reported in 1992 [4, 7, 8].

In the prevalence of MDR strain of S. typhi, a

Correspondence
Dr. Ihsan Ullah
Associate Professor
Department of Microbiology, Institute of Pathology and Diagnostic Medicine, Khyber Medical University, Peshawar - Pakistan
Cell: +92-313-9558883
Email: drihsan.ibms@kmu.edu.pk
Date Received: 23-12-2021
Date Revised: 21-09-2022
Date Accepted: 25-09-2022

geographic variation was observed during a surveillance study, a high prevalence of MDR strain was found in India, Pakistan, and Nepal while a decline rate was observed in China and Bangladesh, and Vietnam [1, 9]. Most of the Asian countries reported a decline in the incidence rate of MDR S. typhi, but unfortunately, the trend of drug resistance increases in Pakistan [10]. With the decline of MDR S. typhi in most of the South Asian countries, some researchers are working on the reuse and effectiveness of the first-line antibiotics again. This may require careful evaluation during clinical practice before it is started for the treatment of enteric fever [3, 11]. However, the resistance against fluoroquinolone is still very high, more than 90% in Pakistan, Bangladesh, India, and Nepal for the last several years [2, 12, 13].

With the rise in antibiotic resistance particularly against Ceftriaxone and fluoroquinolones, there are limited treatment options for S. typhi. Furthermore, the emergence of extensive drug resistant strains limited the available treatment options for S. typhi. XDR strains are resistant to fluoroquinolones and ceftriaxone in addition to first-line drugs [1, 9, 10].

These strains not only cause severe infection but also prolong hospital stay, cost of treatment and mortality among the infected individual [14]. The situation is alarming in the developing countries especially in the rural areas where the latest antibiotics are out of public reach (either expensive or not available) [15].

Physicians treat patients empirically based on their clinical diagnosis[16], and never consider culture and sensitivity either due to lack of the facility, or cost. These factors contribute to the underreporting of actual blood culture-positive typhoid cases [17, 18].

Although typhoid fever is endemic in most of the South Asian countries, however population-based antimicrobial resistance surveillance is lacking. The surveillance study conducted by "surveillance for enteric fever in Asia Project" (SEAP) was a large (2016-2019), and multicenter study which included Pakistan to report the actual picture of S. typhi infection.

In Pakistan, urban areas of Sindh and Punjab got some attention [19] however, data from rural areas of Khyber Pakhtunkhwa and Baluchistan is limited regarding the prevalence and antimicrobial susceptibility profile S. typhi. Therefore, the current study was designed to determine the frequency of enteric fever and antibiotic resistance patterns of S. typhi at a rural district Buner of Khyber Pakhtunkhwa.

MATERIALS & METHOD

This cross-sectional study was conducted at district hospital and some private labs of district Buner Khyber Pakhtunkhwa from Jan 2020 to May 2021. Patients of all age groups visiting hospital for fever at OPD and those admitted were included in the study. For indoor patient suspected or blood culture-confirmed case of enteric fever was included.

For the outdoor patient, those who advise blood culture and had a febrile illness fever for 3-7 days. Patients with known other cause of fever and those already on antibiotics were excluded. Ethical approval was obtained from the institutional ethical committee and an informed written consent was obtained from patients.

Blood samples for culture were collected using aseptic technique to avoid contamination. The blood samples were transferred to a blood culture media bottle (Oxoid) and incubated for 24 hours at 37°C.

After incubation, the blood samples were processed on BACTEC automated system. After that, gram staining was done for the positive samples and then cultured on blood agar, chocolate agar and MacConkey agar for colonial morphology and strain identification, Later the S. typhi was confirmed by serology testing where a multivalent antiserum (BD Difco TM Salmonella) was used against the H, O, and Vi antigens.

All positive isolates were tested for their antimicrobial susceptibility as per Clinical and Laboratory Standard Institute Guideline M100-ED-31, 2021. All those isolates were considered MDR if they show resistance to first-line drugs (Ampicillin/Amoxicillin, Cotrimoxazole, and Chloramphenicol) but susceptible to Fluoroquinolone. On the other hand, if the isolate shows resistance to first-line drugs plus third-generation Cephalosporin and Fluoroquinolone then they were considered extensive drugs resistant (XDR).

All data including socio-demographic information were entered in to a structure proforma. Descriptive analyses such as antimicrobial resistance by age, gender were calculated.

RESULTS

A total of 240 suspected blood samples were collected for S. Typhi isolation from Jan 2020 to May 2021. Out of 240 samples, 98(40.8%) showed growth of S. Typhi on culture media. Staph aureus was 6 (0.025%), Acinetobacter 3(0.012%), and E.coli 2(0.008%). A high prevalence of enteric fever was reported during the month of May to July.

Infection frequency of the study population was assessed over different age groups. The most common age group was between 31-40 years of age, however, age group 21-30 years also showed a high prevalence. The age and gender distribution of S. typhi infection is shown in table 1. Antimicrobial susceptibility profile of S. typhi; was assessed for all positive samples. Samples were streaked on Muller Hinton agar and nine commonly used

antibiotics were tested according to the CLSI guidelines 2020. The isolated S. typhi strains showed 100% resistance to Aztreonam and Ampicillin while they were 100% sensitive to Meropenem and Azithromycin as shown in the figure 1.

Furthermore, sensitivity of 10 samples from the XDR strains was tested against Clarithromycin, where 5 samples showed resistance. Similarly 7 samples from the XDR strains were tested against Vancomycin where 4 samples showed resistance. The Overall the frequency of MDR, XDR and non-MDR strains is shown in table 2

Table 1: Age and gender-wise frequency of S. typhi infection.

Age group/ Gender	≤ 10 Years	11 - 20 Years	21 - 30 Years	31 - 40 Years	41 - 50 Years	51 - 60 Years	61 - 70 Years	70 - 80 Years	Total
Males	5	12	12	9	3	3	2	2	48
Females	1	10	13	14	7	2	2	1	50
Total	6	22	25	23	10	5	4	3	95

Table 2: Frequency of Multi Drugs Resistant (MDR) and Extended Drug Resistant (XDR) strains (n=98).

Resistance pattern	Frequency	Percentage
Multi-drug Resistant	28	%28.6
Extended-drug Resistant	17	%17.4
Non-MDR*/XDR*	53	%54.0
Total	98	100

*MDR- multidrug resistant

*XDR- extended drug resistant

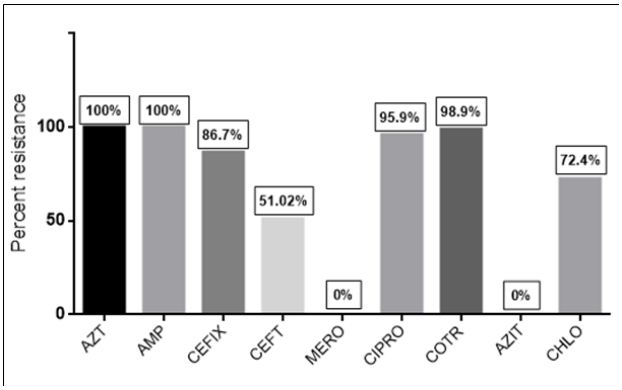

Fig 1: Percent antibiotic resistance of S.typhi

AZT=Aztreonam, AMP=Ampicillin, CEFIX=Cefixime, CEFT=Ceftriaxone, MERO=Meropenem, CIPRO=Ciprofloxacin, COTR=Cotrimoxazole, AZIT=Azithromycin, CHLO=Chloramphenicol

DISCUSSION

Typhoid fever is endemic in some parts of Khyber Pakhtunkhwa, however the resistant strains have increased recently due to the overuse of antibiotics. This study was carried out in a remote area of the Khyber Pakhtunkhwa, district Buner. If the resistant strains are increasing with such high rate, we would have no antibiotics to treat S. typhi in the near future.

In this study we found that S. typhi infection was seen in all age groups however, a high prevalence of enteric fever was reported in middle-aged people between 31-40 years and 21-30 years respectively. Similarly, cases were reported more in females as compared to males. A study conducted by Karkey et al. showed that the prevalence was more between 15-30 years of age which supported our findings, however there were more male patients which is against our findings[20]. This may be because some cultural differences as well as difference in hand hygiene practices of our rural females. Our study found that cases are reported more in May to July of the year due to monsoon rainy season when the sewage water contaminates drinking water, the main source of the enteric pathogen. A similar study conducted at Ghana Hoho Municipality, where the incident rate of enteric fever was higher in June to august while most reported age was found 20 to 35 years, females were found more affected than male [21]. Similarly, another study conducted in Karachi, Pakistan showed that cases occur more during May to August, however they reported higher rate of infection in children [22].

In our study most of the isolates were found resistant to first-line drugs. There was 100% resistance against Aztreonam and Ampicillin, followed by 98.9%, 97%, 72%, and 52% against Cotrimoxazole, Ciprofloxacin, Chloramphenicol, and Ceftriaxone respectively while there was 100% sensitivity to Meropenem and Azithromycin. A study conducted by Shah et al. in 2020 showed nearly the same results and support our findings of the present study [23].

Similarly, some strains of S. typhi were tested against Vancomycin and Clarithromycin and resistance was reported. These drugs are not commonly prescribed in Pakistan, however, resistance is shown against these drugs also which is alarming. The available treatment options for endemic resistant strain of S. typhi are Meropenem and Azithromycin which showed 100% sensitivity.

Studies conducted in Karachi and Hyderabad, Pakistan also showed similar findings of antimicrobial resistance where S. typhi was resistant to most of the antibiotics while there was around 100 % sensitivity to Azithromycin and Meropenem [10, 19, 24] Now-a days the drug of choice is Azithromycin oral or Meropenem intravenous in the hospitalized patients [1, 24], these findings also support our study.

We reported a high prevalence (18%) of XDR along with 28% MDR strains, and our finding was similar to another study conducted in Pakistan [25]. The high prevalence of XDR and MDR is due to misuse of antibiotic either because of self-medication, lack of relevant knowledge, or the influence of medicine companies that facilitate physician by a different mean to sell their product which directly affects the poor community.

CONCLUSION

Our study concludes that resistance to antimicrobial agents is increasing against Salmonella typhi which makes the situation more alarming keeping treatment option limited. The only treatment option left for the endemic strain of S. typhi is Azithromycin and Meropenem. Physicians need to prescribe medication carefully after culture sensitivity to overcome the growing resistance. This study highlights the importance of surveillance study of antimicrobial susceptibilities against S. typhi which would help to set an effective preventive and control measure. Furthermore, the use of the typhoid vaccine must be made available to the local community to lower the burden of antibiotics.

REFERENCES

1. Klemm EJ, Shakoor S, Page AJ, Qamar FN, Judge K, Saeed DK, et al. Emergence of an Extensively Drug-Resistant Salmonella enterica Serovar Typhi Clone Harboring a Promiscuous Plasmid Encoding Resistance to Fluoroquinolones and Third-Generation Cephalosporins. mBio. 2018;9(1).
2. Britto CD, Wong VK, Dougan G, Pollard AJ. A systematic review of antimicrobial resistance in Salmonella enterica serovar Typhi, the etiological agent of typhoid. PLoS neglected tropical diseases. 2018;12(10):e0006779.
3. Gibani MM, Britto C, Pollard AJ. Typhoid and paratyphoid fever: a call to action. Current opinion in infectious diseases. 2018;31(5):440-8.
4. Das JK, Hasan R, Zafar A, Ahmed I, Ikram A, Nizamuddin S, et al. Trends, Associations, and Antimicrobial Resistance of Salmonella Typhi and Paratyphi in Pakistan. The American journal of tropical medicine and hygiene. 2018;99(3_Suppl):48-54.
5. Saeed N, Usman M, Khan EA. An Overview of Extensively Drug-resistant Salmonella Typhi from a Tertiary Care Hospital in Pakistan. Cureus. 2019;11(9):e5663.
6. Bhetwal A, Maharjan A, Khanal PR, Parajuli NP. Enteric Fever Caused by Salmonella enterica Serovars with Reduced Susceptibility of Fluoroquinolones at a Community Based Teaching Hospital of Nepal. International journal of microbiology. 2017;2017:2869458.
7. Parry CM, Ribeiro I, Walia K, Rupali P, Baker S, Basnyat B. Multidrug resistant enteric fever in South Asia: unmet medical needs and opportunities. BMJ (Clinical research ed). 2019;364:k5322.
8. Mutai WC, Muigai AWT, Waiyaki P, Kariuki S. Multi-drug resistant Salmonella enterica serovar Typhi isolates with reduced susceptibility to ciprofloxacin in Kenya. BMC microbiology. 2018;18(1):187.
9. Djeghout B, Saha S, Sajib MSI, Tanmoy AM, Islam M, Kay GL, et al. Ceftriaxone-resistant Salmonella Typhi carries an IncI1-ST31 plasmid encoding CTX-M-15. Journal of medical microbiology. 2018;67(5):620-7.
10. Qamar FN, Yousafzai MT, Khalid M, Kazi AM, Lohana H, Karim S, et al. Outbreak investigation of ceftriaxone-resistant Salmonella enterica serotype Typhi and its risk factors among the general population in Hyderabad, Pakistan: a matched case-control study. The Lancet Infectious diseases. 2018;18(12):1368-76.
11. Rahman M, Ahmad A, Shoma S. Decline in epidemic of multidrug resistant Salmonella typhi is not associated with increased incidence of antibiotic-susceptible strain in Bangladesh. Epidemiology and infection. 2002;129(1):29-34.
12. Zellweger RM, Basnyat B, Shrestha P, Prajapati KG, Dongol S, Sharma PK, et al. A 23-year retrospective investigation of Salmonella Typhi and Salmonella Paratyphi isolated in a tertiary Kathmandu hospital. PLoS neglected tropical diseases. 2017;11(11):e0006051.
13. Barkume C, Date K, Saha SK, Qamar FN, Sur D, Andrews JR, et al. Phase I of the Surveillance for Enteric Fever in Asia Project (SEAP): An Overview and Lessons Learned. The Journal of infectious diseases. 2018;218(suppl_4):S188-s94.
14. Mannan A, Shohel M, Rajia S, Mahmud NU, Kabir S, Hasan I. A cross sectional study on antibiotic resistance pattern of Salmonella typhi clinical isolates from Bangladesh. Asian Pacific journal of tropical biomedicine. 2014;4(4):306-11.
15. Kariuki S, Gordon MA, Feasey N, Parry CM. Antimicrobial resistance and management of invasive Salmonella disease. Vaccine. 2015;33 Suppl 3(0 3):C21-9.
16. Maskey AP, Day JN, Phung QT, Thwaites GE, Campbell JI, Zimmerman M, et al. Salmonella enterica serovar Paratyphi A and S. enterica serovar Typhi cause indistinguishable clinical syndromes in Kathmandu, Nepal. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. 2006;42(9):1247-53.
17. Kothari A, Pruthi A, Chugh TD. The burden of enteric fever. Journal of infection in developing countries. 2008;2(4):253-9.
18. Voysey M, Pant D, Shakya M, Liu X, Colin-Jones R, Theiss-Nyland K, et al. Under-detection of blood culture-positive enteric fever cases: The impact of missing data and methods for adjusting incidence estimates. PLoS neglected tropical diseases. 2020;14(1):e0007805.
19. Qamar FN, Yousafzai MT, Dehraj IF, Shakoor S, Irfan S,

Hotwani A, et al. Antimicrobial Resistance in Typhoidal Salmonella: Surveillance for Enteric Fever in Asia Project, 2016-2019. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. 2020;71(Suppl 3):S276-s84.

20. Karkey A, Arjyal A, Anders KL, Boni MF, Dongol S, Koirala S, et al. The Burden and Characteristics of Enteric Fever at a Healthcare Facility in a Densely Populated Area of Kathmandu. PloS one. 2010;5(11):e13988.
21. Fusheini A, Gyawu SK. Prevalence of Typhoid and Paratyphoid Fever in the Hohoe Municipality of the Volta Region, Ghana: A Five-Year Retrospective Trend Analysis. Annals of global health. 2020;86(1):111.
22. Yousafzai MT, Irfan S, Thobani RS, Kazi AM, Hotwani A, Memon AM, et al. Burden of Culture Confirmed Enteric Fever Cases in Karachi, Pakistan: Surveillance For Enteric Fever in Asia Project (SEAP), 2016-2019. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. 2020;71(Suppl 3):S214-s21.
23. Ali Shah SA, Nadeem M, Syed SA, Fatima Abidi ST, Khan N, Bano N. Antimicrobial Sensitivity Pattern of Salmonella Typhi: Emergence of Resistant Strains. Cureus. 2020;12(11):e11778.
24. Javaid N, Sultana Q, Rasool K, Gandra S, Ahmad F, Chaudhary SU, et al. Trends in antimicrobial resistance amongst pathogens isolated from blood and cerebrospinal fluid cultures in Pakistan (2011-2015): A retrospective cross-sectional study. PloS one. 2021;16(4):e0250226.
25. Hussain A, Satti L, Hanif F, Zehra NM, Nadeem S, Bangash TM, et al. Typhoidal Salmonella strains in Pakistan: an impending threat of extensively drug-resistant Salmonella Typhi. European journal of clinical microbiology & infectious diseases : official publication of the European Society of Clinical Microbiology. 2019;38(11):2145-9.

CONFLICT OF INTEREST: Authors declare no conflict of interest

GRANT SUPPORT AND FINANCIAL DISCLOSURE: NIL

AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under

Ali A:	Principal investigator, Concept and data analysis
Rahman N:	Data handling and critical analysis
Adeeb H:	Manuscript drafting
Ullah I:	Bibliography, Project design, Critical review, analysis of data

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

ORIGINAL ARTICLE

SHORT-TERM OUTCOMES OF OPEN REDUCTION OF DEVELOPMENT DYSPLASIA OF THE HIP BY MEDIAL APPROACH: OUR EXPERIENCE AT KHYBER TEACHING HOSPITAL PESHAWAR

Hamza Zafar, Sikandar Hayat, Yaad zaman, Imran Marwat, Asnaf Siddique, Abdullah

Department of Orthopedics, Khyber teaching hospital Peshawar - Pakistan

ABSTRACT

Objective: Our study aimed to determine the short-term outcome of open reduction by medial approach in terms of function, joint reduction, and avascular necrosis.

Material & Methods: This was a Descriptive study approved by the institutional review board. We performed open reduction by medial approach in 24 hips in children less than 18 months of age. We followed them for a mean of 32 months ± 10.5 months. The average age of surgery was 9.7 months ± 3.5 months.

Results: Out of 24 hips, 22 were successfully reduced and two hips required revision surgery for post-operative redislocation of the hip joint. Avascular necrosis was noted in three hips and functionally classified according to McKay criteria 22 hips showed excellent one hip good, and one hip fair outcome.

Conclusion: We concluded that the medial approach is effective and reliable in achieving good short-term outcomes. It is safe and easy with a low rate of complications performed in children less than 18 months of age.

Keywords: development dysplasia of hip joint, DDH, medial approach, open reduction, short-term follow-up, Avascular necrosis..

This article may be cited as: Zafar H, Hayat S, Zaman Y, Marwat I, Siddique A, Abdullah. Short-term outcomes of open reduction of Development Dysplasia of the hip by medial approach: Our experience at Khyber teaching hospital Peshawar. J Med Sci 2022 July;30(3):190-193

INTRODUCTION

Developmental dysplasia is a spectrum of many overlapping conditions ranging from occult dysplasia to dislocated hip.[1] The hallmark of DDH is acetabular dysplasia which is the abnormality in size, shape, and orientation.[2] The incidence which depends on various factors like gender, race, diagnostic criteria, etc. is between 1.5 and 20%.[3] b Treatment of DDH depends upon age and the goal is to achieve and maintain concentric reduction of the femoral head into the acetabulum. The prognosis is best when treatment is started very early. This has been achieved in developed countries through awareness, Improved training, increased surveillance, and quicker access to pediatric orthopedic surgeons. But in developing countries like Pakistan, the diagnosis is often delayed due to few specialized pediatric orthopedic surgeons, Specialized centers, and a lack of fellowships programs.[4] If the age is less than six months, the Pavlick harness is used. It is monitored by ultrasonography. After six months close reduction with arthrography and hip spica in human position is the procedure of choice. When close reduction fails open reduction is needed which is performed either by an anteromedial or anterolateral approach. Anterolateral is an excellent approach that gives good functional and radiological outcomes in neglected DDH.[5] The anteromedial approach for surgical treatment was first described by Ludloff in 1908, later on, modified by Ferguson and Weinstein, and Ponseti.[6] It is performed in infants between 6-18 months. Open reduction by the medial approach has many advantages including lesser tissue dissection, lower blood loss, shorter surgical duration, and bilateral applicability.

But it has disadvantages too like the inability to evaluate the pathological changes in superior acetabulum and difficulty in capsuloraphy.[7] A long follow-up study showed that if surgery through a medial approach is performed at an appropriate age can give good results in terms of good joint congruity and encourage ideal maturity of the joint.[8] The incidence of Avascular necrosis(AVN) of the femoral head in the medial approach ranges from 0% to 67% is the concern. The medial femoral circumflex artery may be injured during capsulotomy.[(9)] In this study we have evaluated the short-term outcomes of Ludloff's medial approach for an open reduction in terms of the acetabular index and

Correspondence
Dr. Sikandar Hayat
Associate Professor
Department of Orthopedics, Khyber teaching hospital Peshawar
Cell: +92-332-9474849
Email: drsikandar68@gmail.com
Date Received: 13-03-2022
Date Revised: 05-09-2022
Date Accepted: 20-09-2022

concentric reduction and potential complications like AVN of the femoral head. the objective of the current study was to determine the short-term outcomes of open reduction by medial approach for developmental dysplasia of the hip in children less than 18 months of age.

MATERIAL & METHODS

This was a descriptive study. After taking ethical approval from the review board, data collection started with informed consent from the patients treated in Khyber teaching hospital by a single surgeon who specialized in pediatric orthopedic surgery. Data were collected for 6 months duration from April 2021 to December 2021.

The sampling technique was nonprobability consecutive and children below 18 years were selected. Syndromic patients and previously failed surgery for DDH were excluded. Short-term outcomes are defined as an assessment after at least 18 months of follow-up. Those patients who had to follow up for less than 18 months were also excluded from the study. The incidence of DDH is variable in a different population ranging from 1.5% to 20%. In our country, as there is no screening program for at-risk children, the mean age of presentation is above 2 years as reported in previous studies.[10-12]. Therefore, our sample size was small and about 20 hips were included in the study. Data were analysed using spss 21.

We performed routine arthrography before open reduction through a medial approach. Dynamic evaluation of hip joint reduction was evaluated. If congruent hip reduction was not possible Open reduction (OR) of the hip proceeded through the Ludloff approach by 2 to 3 cm transverse incision over the adductor longus muscle. After adductor tenotomy, an intermuscular plan between the pectineus and the adductor brevis was developed. After the iliopsoas tenotomy, just proximal to the lesser trochanter, the anterior surface of the hip joint capsule was exposed. Branches of the medial circumflex artery were visible which are protected to prevent AVN. Capsulotomy with cruciate incision exposed the hip joint to all intra-articular obstacles. Excision of Ligamentum teres, transverse acetabular ligament, and pulvinar performed. Hip was reduced and stability was checked. The skin was closed and hip spica was given in a human position for 6 weeks. After the hip Spica was removed child was placed in a removable hip abduction brace for another 3 months.

RESULTS

We had 16 patients (24 hips) included in our study out of which 11 were female and 5 were male. The mean age of surgery was 9.7 months ± 3.5 months (range from 5 to 18 months). The mean follow-up was 32 months ± 10.5 months (range from 18 to 54 months). Preoperative traction was not used in any case. Out of 16 patients, we had 4 right side involvement, 4 left sides and 8 had bilateral involvement. The reduction was achieved in 22 hips. Two hips got redislocated and required 2nd reduction surgery through an anterolateral approach. Final radiographic outcome at minimum 18 months follows up of all 24 hips shows reduced hip joints marked by congruency and intact Shenton line. We lost the pre-operative data of 9 hips. Out of 15, we had seven hips of tonnis grade 4, 3 hips of grade 3, and 4 hips of grade 2 dislocation. Pre-operative mean acetabular index of 15 hips was 40.1 ± 5.6 (range 30-50) while the mean acetabular index of 24 hips post-op was 23.83 ± 6.81 (range 15 to 37). A postoperative acetabular index of more than 25 degrees was noted in 13 hips which shows hip dysplasia. Avascular necrosis(AVN) was noted in three hips(12.5%) and was classified according to Kalamchi and Mcevan criteria. According to this criteria, one hip had grade 1 AVN and the other two had grade 2 AVN. Functional outcome according to Mckay criteria shows 22 hips (87.5%) excellent outcome. One hip (4.2 %) was good and one hip (4.2 %) fair outcome. We had no hip with a poor outcome. The range of motion of the hip joint was in the normal range in 20 (83%) hips. Three hips showed up to a 10-degree decrease in range of motion and one hip had limited external rotation causing the poor functional outcome.

DISCUSSION

Advantages of the medial approach include minimal invasive technique, less blood loss, less intra-operative time, supine position and both sides can be operated on at the same time, and unnoticeable scar marks. The tight anterior capsule that is the major obstacle in reduction can be released with this approach.[13] Disadvantage of the medial approach is no excess to extra-articular obstacle for reduction that includes posterior adhesion of capsule with the ilium, torsion of the capsule, and contracture of short rotator mussels but some authors consider the main interfering factors to be intra-articular.[8, 14] If the femur head is not reduced properly it will lead to subluxation in early childhood when the patient starts walking.[8] It will need further corrective surgery to achieve better congruency.

The femur head superior subluxation may occur in a centrally reduced head if the surgery is done in an ambulatory child so a medial approach is preferred in non-ambulatory infants.[15] One of the common complications of the medial approach is AVN. The reason is that in this approach one has to dissect and protect the femoral vessel and nerve pack and then the medial circumflex artery and obturator nerve. Medial circumflex artery injury or ligation is the major culprit for post-operative AVN.[16] The incidence of avascular necrosis was 12.5% in our study which was low compared to 42% Koizumi et al[14] 20-year follow-up, 41% morcuende et al[17] means 11 years follow-up, and 35.5% sosna et al[18] mean 11 years follow up respectively. The reason for our low AVN rate is a short-term follow-up (mean 30 months).

Iyetin et all[16] reported 3.6% AVN in 41 patients treated by medial approach with a mean follow-up of 5.5 years. Some authors suggest that AVN is not caused by the surgery but by the use Pavlik harness before the surgery.[18] Hip spica in flexion abduction also increases the risk of AVN.[19] In our study we give hip spica for up to 6 weeks. The average rate of 2nd operation required for pa-

Table 1: All cases included in the study with clinical and radiological outcome.

Hip no	Age at operation (months)	Gender Male(M)Female(F) /side	Last followup (months)	Pre-operative Acetabular index	Acetabular index last followup	Functional outcome Mckay Criteria	Avascular necrosis
1	12	F / left	36	35	20	excellent	No
2	11	M / left	24	35	15	excellent	Grade 2
3	10	F / right	50	45	20	Excellent	No
4	10	F / left	50	45	35	Excellent	No
5	10	F / left	20	45	20	Excellent	No
6	5	F / right	31	40	20	Excellent	No
7	5	F / left	31	30	20	Excellent	No
8	12	M / right	36	40	15	Excellent	No
9	12	M / left	36	30	30	Excellent	Grade 1
10	10	F / right	50	50	15	Fair	Grade 2
11	10	F / right	38	40	25	Excellent	No
12	9	M / right	34		20	Excellent	No
13	9	M / left	34		20	Excellent	No
14	6	F / right	21	40	23	Excellent	No
15	6	F / left	21	45	28	Excellent	No
16	8	F / right	27		30	Excellent	No
17	9	F / left	26		35	Excellent	No
18	6	F / right	18		19	Excellent	No
19	6	F / left	18		26	Excellent	No
20	18	M / right	54	40	26	Excellent	No
21	15	F / left	42	42	37	Excellent	no
22	6	F / right	36		24	Excellent	No
23	14	F / left	30		15	Good	no
24	16	M / left	27		34	Excellent	no

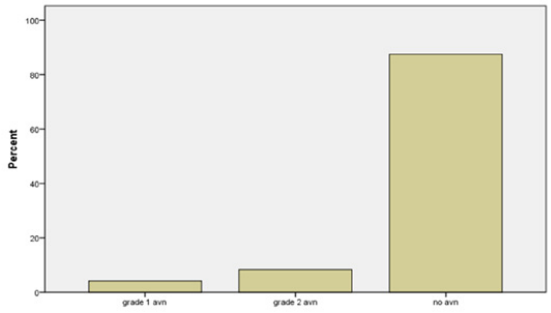

Fig 1: Percentage of Avascular necrosis according to Kalmachi and Mcevan criteria

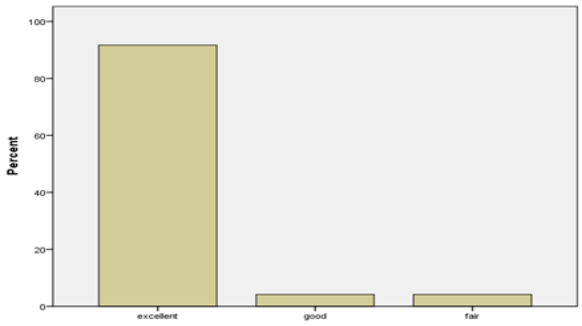

Fig 2: Percentage of Functional outcome according to Mckay criteria

tients treated by the medial approach is from 0 to 53% and the average rate of re-dislocation is from 0 to 23%.[17,18,20-22] We had two cases of re-dislocation in our study. The reason can be less expertise of the surgeon or may be due to loss of reduction in spica. We reduced them with an anterolateral approach and the patient outcome is good. The limitation of our study was that it was a single-center study with a small sample size. The follow-up period was short-term with a mean of 30 months and as the child grows the acetabulum remodels so the outcome can be assessed more accurately by long-term follow-up. The common complication of the Medial approach is late Kalamachi and Mcevan AVN type 2 which usually do not show themselves until 10 years. Long-term follow-up with a large sample size study is required to evaluate more precise outcomes of these patients.

CONCLUSION

The medial approach is a safe and easy approach to reducing hip joints in patients less than 18 months of age. The short-term outcomes are satisfactory and both hips can be addressed in one anesthesia session.

REFERENCES

1. Jain R, Patel S. Developmental dysplasia of hip–An overview. International Journal of Orthopaedics. 2017;3(4):42-9.
2. Spasovski D. Introductory Chapter: Five-Dimensional Approach to the Developmental Dysplasia of the Hip. Developmental Diseases of the Hip-Diagnosis and Management: IntechOpen; 2017.
3. Li L, Zhang L, Li Q, Zhao Q, Jia J, Huang T. Development of the osseous and cartilaginous acetabular index in normal children and those with developmental dysplasia of the hip: a cross-sectional study using MRI. The Journal of Bone and Joint Surgery British volume. 2012;94(12):1625-31.
4. Noordin S, Umer M, Hafeez K, Nawaz H. Developmental dysplasia of the hip. Orthop Rev (Pavia). 2010;2(2).
5. Glorion C. Surgical reduction of congenital hip dislocation. Orthopaedics & Traumatology: Surgery & Research. 2018;104(1):S147-S57.
6. Ozkut AT, Iyetin Y, Unal OK, Soylemez MS, Uygur E, Esenkaya I. Radiological and clinical outcomes of medial approach open reduction by using two intervals in developmental dysplasia of the hip. Acta Orthop Traumatol Turc. 2018;52(2):81-6.
7. Türközü T, Güner S, Ceylan MF, Güven N. The outcomes of open reduction by the medial approach for developmental dysplasia of the hip in the 3-18 months old patients. Eastern Journal Of Medicine. 2017;22(2):39.
8. Yamada K, Mihara H, Fujii H, Hachiya M. A long-term follow-up study of open reduction using Ludloff's approach for congenital or developmental dislocation of the hip. Bone & joint research. 2014;3(1):1-6.
9. Farsetti P, Caterini R, Potenza V, Ippolito E. Developmental dislocation of the hip successfully treated by preoperative traction and medial open reduction: a 22-year mean followup. Clinical Orthopaedics and Related Research®. 2015;473(8):2658-69.
10. Zimri FUK, Shah SSA, Saaiq M, Qayyum F, Ayaz M. Presentation and Management of Neglected Developmental Dysplasia of Hip (DDH): 8-years' experience with single stage triple procedure at National Institute of Rehabilitation Medicine, Islamabad, Pakistan. Pakistan Journal of Medical Sciences. 2018;34(3):682.
11. Bhatti A, Kumar J, Butt SA. Outcome of one stage combined open reduction, pelvic and derotation femoral osteotomy in congenital dislocated hips of children younger than three years age. J Pak Med Assoc. 2014;64(9):1015-20.
12. ur Razaq MN, Younas M, Awan AS, Waqas M, Alam MI, ullah Khan I. Risk factors leading to developmental complications after open reduction in developmental dysplasia of hip. Journal of Ayub Medical College Abbottabad. 2016;28(1):26-8.
13. Weinstein S, Dolan L. Proximal femoral growth disturbance in developmental dysplasia of the hip: what do we know? Journal of children's orthopaedics. 2018;12(4):331-41.
14. Kotlarsky P, Haber R, Bialik V, Eidelman M. Developmental dysplasia of the hip: What has changed in the last 20 years? World journal of orthopedics. 2015;6(11):886.
15. Gabuzda G, Renshaw T. Reduction of congenital dislocation of the hip. Journal of Pediatric Orthopaedics. 1992;12(6):830.
16. Iyetin Y, Turkmen I, Saglam Y, Akcal MA, Unay K, Unsac B. A modified surgical approach of the hip in children: is it safe and reliable in patients with developmental hip dysplasia? J Child Orthop. 2015;9(3):199-207.
17. Morcuende JA, Meyer MD, Dolan LA, Weinstein SL. Long-term outcome after open reduction through an anteromedial approach for congenital dislocation of the hip. JBJS. 1997;79(6):810-17.
18. Cooper AP, Doddabasappa SN, Mulpuri K. Evidence-based management of developmental dysplasia of the hip. Orthopedic Clinics. 2014;45(3):341-54.
19. Gardner R, Bradley C, Howard A, Narayanan U, Wedge J, Kelley S. The incidence of avascular necrosis and the radiographic outcome following medial open reduction in children with developmental dysplasia of the hip: a systematic review. The Bone & Joint Journal. 2014;96(2):279-86.
20. Bradley CS, Perry DC, Wedge JH, Murnaghan M, Kelley SP. Avascular necrosis following closed reduction for treatment of developmental dysplasia of the hip: a systematic review. Journal of children's orthopaedics. 2016;10(6):627-32.
21. Kalamchi A, SCHMIDT TL, MACEWEN GD. Congenital Dislocation of the Hip: Open Reduction by the Medial Approach. Clinical Orthopaedics and Related Research (1976-2007). 1982;169:127-32.
22. Novais EN, Hill MK, Carry PM, Heyn PC. Is age or surgical approach associated with osteonecrosis in patients with developmental dysplasia of the hip? A meta-analysis. Clinical Orthopaedics and Related Research®. 2016;474(5):1166-77.

CONFLICT OF INTEREST: Authors declare no conflict of interest

GRANT SUPPORT AND FINANCIAL DISCLOSURE: NIL

AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under

Authors contribution

Zafar H:	Proposal, data collection, writing
Hayat S:	Concept, data collection, writing
Zaman Y:	Writing, review, data collection
Marwat I:	Data collection, review
Siddique A:	Data collection
Abdullah:	Data collection

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

ORIGINAL ARTICLE

FREQUENCY AND IN-HOSPITAL MORTALITY OF RIGHT VENTRICULAR MYOCARDIAL INFARCTION IN PATIENTS WITH INFERIOR WALL MYOCARDIAL INFARCTION

Shoaib Subhan[1], Yasir Arafat[2], Jibran Umar Ayub Khan[3], Hikmatullah Jan[1], Ayesha Qaisar[4], Azhar Zahir Shah[5]

[1]Department of Cardiology Kabir Medical College, Peshawar - Pakistan

[2]Department of Cardiology Qazi Hussain Medical Complex, Nowshera Medical College Nowshera, Peshawar - Pakistan

[3]Department of Medicine Kabir Medical College Peshawar - Pakistan

[4]Department of Physiology Khyber Medical College, Peshawar - Pakistan

[5]Department of Surgery, Sardar Begum Dental College Peshawar, Peshawar - Pakistan

ABSTRACT

Objective: To determine the frequency and in-hospital mortality of right ventricular myocardial infarction, in patients with inferior wall myocardial infarction.

Material & Methods: This was a descriptive case series, conducted at Cardiology Department, Rehman Medical institute during time duration 18th Feb 2017 to 18th Aug 2017. The study was conducted after approval was obtained from the hospital ethical review committee. Sample selection was done through a non-probability consecutive sampling technique. Patients were included in the study based on inclusion and exclusion criteria

A detailed history was taken followed by a complete physical examination and ECG was done. Demographic and outcome data were noted on a predesigned Performa.

Results: The mean age (SD) of patients in this study was 68±11.05 years. 94 (60.64%) patients were male while 61 (39.35%) patients were female. Among patients 142 (91.61%) were smokers, 136 (87.74%) patients were hypertensive and 123 (79.35%) patients were diabetic. A total of 155 patients were hospitalized with the diagnosis of acute inferior STEMI. Of the total 155 in-patients, 56(36.1%) were having right ventricular infarction. In-hospital mortality was recorded in 39/155(25.16%) patients during hospitalization having right ventricular myocardial infarction with inferior wall myocardial infarction.

Conclusion: This study concluded that Right Ventricular Infarction can occur in patients with Inferior Wall Myocardial Infarction with certain adverse in-hospital outcomes such as mortality.

Keywords: Coronary Artery Disease (CAD), Right Ventricle Infarction (RVI).

This article may be cited as: Subhan S, Arafat Y, Khan JUA, Jan H, Qaisar A, Shah AZ. Siddique A, Frequency and In-hospital Mortality of Right Ventricular Myocardial Infarction in Patients with Inferior Wall Myocardial Infarction. J Med Sci 2022 July;30(3):194-197

INTRODUCTION

Acute coronary syndrome (ACS) is the leading cause of morbidity and mortality in men and women all over the world which accounts for 16.7 million deaths yearly despite the advancement in cardiovascular medicine and intervention and preventive strategies in coronary artery disease[1, 2]. The prevalence of ACS in Pakistan is increasing rapidly due to increased risk factors for atherosclerosis, which account for more than 100,000 (12%) of the total death annually[3].

Anterior wall myocardial infarction (AWMI) has a destructive course, but acute inferior wall myocardial infarction (IWMI) can also be risky, especially if it involves the right ventricle. Right ventricular infarction (RVI) can severely interfere with hemodynamics, conduction, and Valvular irregularities, which can result in sudden death[4]. Clinically RVI is characterized by raised JVP, bilateral clear lungs, and systemic arterial hypotension(5). It is usually caused by proximal R.C.A occlusion before its RV branch. Acute IWMI account for 40 to 50% of all types of myocardial infarctions(6) which has better short and long-term prognosis, accounting for 8% mortality and mortality increases to 30% when accompanied by RVI[7]. Even in-hospital mortality in elderly patients reaches up to 50% with

Correspondence
Dr. Jibran Umar Ayub Khan
Assistant Professor
Department of Medicine Kabir Medical College, Peshawar -Pakistan
Cell: +92-333-9227301
Email:jibranumar@yahoo.com
Email: drsikandar68@gmail.com
Date Received: 13-03-2022
Date Revised: 05-09-2022
Date Accepted: 20-09-2022

the involvement of RVI[7]. RVI complicates 20 to 50% of acute IWMI reported by multiple studies[7-9] . The frequency of RVI in acute IWMI is reported to differ in many studies. A study by Ravikeerthy M et al and Memon AG et al observed an increased incidence of RVI which is 40 % and 48.5 % respectively[10, 11].

This study will help determine the local burden of inferior wall MI with RV infarction and its in-hospital mortality and thus helping us in early detection and timely management according to Guidelines Determined Medical Therapy thus reducing mortality and furthermore providing us local Data.

MATERIAL & METHODS

This was a Descriptive cross-sectional study carried out at Cardiology Department, Rehman Medical Institute, Peshawar from 18th Feb 2017 to 18th Aug 2017. A total sample size of 155 patients was calculated keeping a proportion of 27% of-hospital mortality from right ventricular infarction in patients with inferior wall Myocardial infarction keeping a confidence level of 95% margin of error of 7% using the WHO calculator20. Sample selection was done through non-probability consecutive sampling. Patients were included in the study based on the following inclusion and exclusion criteria.

All hospitalized patients with the diagnosis of acute inferior STEMI of either gender between ages 40-80 years were included. All patients with acute inferior STEMI and RV infarction who die within a week in hospital (because of RV infarction in inferior wall MI). Exclusion criteria were patients with a previous history of diagnosed right ventricular infarction.

The study was conducted after approval is obtained from the hospital ethics research committee. All patients with acute inferior STEMI diagnosed by meeting the inclusion criteria were enrolled in the study, through the outpatient or emergency department. Written informed consent was obtained after explaining the purpose and benefits of the study.

All patients were admitted to the cardiology unit of the hospital for further evaluation. A detailed history was taken followed by a complete physical examination. ECG was done by using the Toshiba 1Aplio 2Xario 3Core Vision and Perlong SXD-3A1 Machines to avoid confounders and bias.

All the above information including name, age, and gender, was recorded in a predesigned Performa. Exclusion criteria were followed strictly to control confounders and bias in the study results. Those having right ventricular infarction were noted and any death in these patients was recorded. In-hospital mortality was defined as patients who were being diagnosed with inferior wall MI having RV infarct and who die within a week in hospital based on hospital records (because of RV infarct).

DATA ANALYSIS PROCEDURE

Data was entered into SPSS version 19. Mean± standard deviation was calculated for numerical variables like age and duration of disease. Frequencies and percentages were calculated for categorical variables like gender in-hospital mortality. In-hospital mortality was stratified among age, gender, smoking (10 cigarettes per day in last one year), hypertension (from last 2 years), diabetes (known diabetic from last 2 years), site of occlusion of Right coronary artery, and duration of disease to control the effect modifier. Post-stratification was done through a Chi-square test keeping P valve < 0.05 as significant.

RESULTS

In this study mean age of patients in this study was 68±11.05 years. 94 (60.64%) patients were male while 61 (39.35%) patients were female. Among patients 142 (91.61%) were smokers, 136 (87.74%) patients were hypertensive and 123 (79.35%) patients were diabetic. In-hospital mortality was recorded in 39(25.16%) patients during hospitalization having right ventricular myocardial infarction with inferior wall myocardial infarction.

Table 1: Patients characteristics (n=155).

	Frequency	Percent
Age	68±11.05 years	
Male	94	60.64%
Female	61	39.35%
Smoker	142	91.61%
Hypertensive	19	12.25%
Diabetes	123	79.35%
Hospital Mortality	39	25.16%
Right ventricular infarction	56	36.1%

Table 2: Mortality in relation to Patients characteristics.

		Mortality		p-value
		Yes (n=39)	No (n=116)	
Age (Years)	40-50	3(1.93%)	14(9.03%)	p-value
	51-60	12(7.74%)	39(25.16%)	
	61-70	8(5.16%)	22(14.19%)	
	71-80	16(10.32%)	41(26.45%)	
Gender	Male	20(12.90%)	74(47.74%)	0.831
	Female	19(12.25%)	42(27.09%)	
Smoking	Yes	37(23.87%)	105(67.74%)	0.1667
	No	2(1.29%)	11(7.09%)	
HTN	Yes	5(3.22%)	102(65.08%)	0.396
	No	34(21.93%)	14(9.03%)	
Diabetes	Yes	34(21.93%)	89(57.41%)	<0.001
	No	5(3.22%)	27(17.41%)	

DISCUSSION

The importance of early recognition of RVI lies in the fact that, having a correct diagnosis can lead to more appropriate treatment instituted quickly to avoid hypotension i.e. intravenous fluid administration and thrombolysis, with streptokinase can be given because of higher mortality in this group of patients. In the current study, 36.1% of patients had right ventricular infarction along with acute inferior wall MI which stressed the early recognition of right ventricular infarction to decrease in-hospital morbidity and mortality.

A recent study in Karachi Pakistan by Hassam et al reported a 36% prevalence of RVI in the setting of acute IWM which is a similar finding to our study result[12]. while in another study it was reported as 30%, which was less than our study result and study finding by Hassam et al[13]. In contrast to our study result finding A study by Ravikeerthy M et al and Memon AG et al observed an increased incidence of RVI which is 40 % and 48.5 % respectively which is far higher than our study result[10,].

Among the diseases of the coronary arteries, ST-elevation myocardial infarction (STEMI) causes high morbidity and mortality. STEMI may involve either the anterior, inferior, and/or posterior wall of the heart. Acute myocardial infarction (AMI) involving only the right ventricle is a rare event[14]. Much more often, the right ventricular infarction is associated with infarction of the inferior wall of the left ventricle, affecting more than one-third of these cases. In these patients, myocardial infarction usually involves the posterior-inferior wall, septum, and posterior right ventricular free wall[14]. Hemodynamically significant myocardial infarction occurs almost exclusively in patients with inferior infarction[14].

Ischemia or infarction of the right ventricle can lead to a decrease in right ventricular compliance, reduced filling, and reduced stroke volume of the right side with right ventricular concomitant dilation and modification of the septal curvature[15]. These hemodynamic and geometrical changes can lead to reduced left ventricular filling and cardiac contractile function with a concomitant decrease in cardiac output[15, 16]. The net effect is that the filling pressures of the left side may be below normal despite clinical signs of high pressure on the right side. This disparity has important implications for treatment.

Recognizing the right ventricular infarct in the acute setting is important because management is quite different from the anterior wall myocardial infarction. Previously, most patients with acute coronary syndrome and chest pain receive nitrates in addition to standard treatment. Nitrates are contraindicated in patients with RV infarction; instead, they are given fluids to increase the filling pressure of the right side of the heart to maintain cardiac output[17, 18].

RV involvement in inferior MI is associated with increased early morbidity and mortality. In one study it was shown that RV infarct is an independent risk factor for increased mortality even in this era of primary percutaneous intervention[19, 20]. In one study recently done, it was shown that in-hospital mortality varies from 27% to 80 % depending on whether or not a patient received reperfusion therapy[21]. There is more myocardial damage in patients having inferior wall MI with RV infarction[20].

A study by Saif M et al reported 20(7.7%) mortality out of 261 patients who received PCI for acute inferior wall mi with RV infarct which was far lower than 39 (25.16%) than our study result[21].In contrast, a study by Kukla P et al reported 18.5% mortality in a patient with RVI which is about nearly to our result finding[23]. In Pakistan, only a single study mentioned above was published on the frequency of right ventricular infarction in the inferior wall MI. This study has helped us determine the local burden of inferior wall MI with RV infarction and its-hospital mortality.

The main limitation of the study is the single center and small sample size, and their result cannot be generalized. Descriptive studies cannot be used to establish cause-and-effect relationships. Respondents may not be truthful when answering the questions or may give socially desirable responses.

CONCLUSION

This study concluded that Right Ventricular Infarction can occur in patients with Inferior Wall Myocardial Infarction with certain adverse in-hospital outcomes

REFERENCES

1. Virani SS, Alonso A, Benjamin EJ, Bittencourt MS, Callaway CW, Carson AP, et al. Heart disease and stroke statistics—2020 update: a report from the American Heart Association. Circulation. 2020;141(9):e139-e596.
2. Ahmed S, Ahsan M. Ehsan Ullah. Stable angina: the frequency of coronary artery stenosis among patients having left bundle branch block Professional Med J. 2009;16:94-9.
3. Kazim SF, Itrat A, Butt NW, Ishaq M. Comparison of cardiovascular disease patterns in two data sets of patients admitted at a Tertiary Care Public Hospital in Karachi five years apart. Pak J Med Sci. 2009;25(1):55-60.
4. Saleh M, Ambrose JA. Understanding myocardial infarction. F1000Research. 2018;7:1000-378.
5. O'ROURKE RA. Diagnosis and management of right ventricular myocardial infarction. Curr Probl Cardiol. 2004;29:6-47.
6. Group I-C. Randomized trial of intravenous streptokinase, oral aspirin, both, or neither among 17,187 cases of suspected acute myocardial infarction: ISIS-2. J Am Coll Cardiol. 1988;12(6SA):A3-A13.
7. Kukla P, Dudek D, Rakowski T, Dziewierz A, Mielecki W, Szczuka K, et al. Inferior wall myocardial infarction with

or without right ventricular involvement: treatment and in-hospital course. Kardiol Pol. 2006;64(6) :583-588

8. Gumina R, Wright R, Kopecky S, Miller W, Williams B, Reeder G, et al. Strong predictive value of TIMI risk score analysis for in-hospital and long-term survival of patients with right ventricular infarction. Eur. Heart J. 2002;23(21):1678-83.
9. Aguiar Rosa S, Timóteo AT, Ferreira L, Carvalho R, Oliveira M, Cunha P, et al. Complete atrioventricular block in acute coronary syndrome: prevalence, characterisation and implication on outcome. Eur. Heart J. Acute Cardiovasc. Care. 2018;7(3):218-23.
10. Ravikeerthy M, Yogi S. A study of right ventricular infarction in inferior wall myocardial infarction. Int J Sci Res Publ. 2015;5(4): 120-4
11. Memon AG, Shah MI, Devrajani BR, Baloch S. Incidence of right ventricular infarction in patients with acute inferior wall infarction. J Postgrad Med Inst 2015; 29(3): 189-92
12. Ali H, Sarfraz S, Fawad M, Shafique Z. Frequency of right ventricular infarction in inferior wall myocardial infarction. Cureus. 2020;12(5): e8238.
13. Khandait V, Sarwale S, Atkar C, Khandait H. Clinical profiling of right ventricular infarction in patients with acute inferior wall myocardial infarction. Int J Adv Med. 2019;6(1):35-9.
14. Rathore SS, Gersh BJ, Weinfurt KP, Oetgen WJ, Schulman KA, Solomon AJ. The role of reperfusion therapy in paced patients with acute myocardial infarction. Am Heart J. 2001; 142(3):516-9.
15. Jaffe AS. Third universal definition of myocardial infarction. ClinBiochem. 2013; 46 (1-2):1-4.
16. Bonaca MP, Wiviott SD, Braunwald E, et al. American College of Cardiology/American Heart Association/European Society of Cardiology/World Heart Federation Universal definition of myocardial infarction classification system and the risk of cardiovascular death: observations from the TRITON-TIMI 38 Trial (Trial to Assess Improvement in Therapeutic Outcomes by Optimizing Platelet Inhibition With Prasugrel-Thrombolysis in Myocardial Infarction 38). Circulation. 2012; 125(4):577-83.
17. Kolodgie FD, Virmani R, Burke AP, et al. Pathologic assessment of the vulnerable human coronary plaque. Heart. 2004; 90 (12):1385-91.
18. Chatzizisis YS, Coskun AU, Jonas M, Edelman ER, Feldman CL, Stone PH. Role of endothelial shear stress in the natural history of coronary atherosclerosis and vascular remodeling: molecular, cellular, and vascular behavior. J Am CollCardiol. 2007; 49(25):2379-93.
19. Wang JC, Normand SL, Mauri L, Kuntz RE. Coronary artery spatial distribution of acute myocardial infarction occlusions. Circulation. 2004; 110(3):278-84.
20. Falk E, Shah PK, Fuster V. Coronary plaque disruption. Circulation. 1995 Aug 1. 92(3):657-71. McDaniel MC, Willis P, Walker B, et al. Plaque necrotic core content is greater immediately distal to bifurcations compared to bifurcations in the proximal lad of patients with CAD. Am J Cardiol. 2008;102(8):242i.
21. Yusuf S, Hawken S, Ounpuu S, et al, for the INTERHEART Study Investigators. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. Lancet. 2004; 364 (9438):937-52.
22. Saif M, Safi SI, Samin A, Bukhari J, Khan S. frequency of right ventricular infarction and in-hospital outcome after primary percutaneous coronary intervention (ppci) in acute inferior myocardial infarction (mi). j Armed Forces Med Coll. 2020;70(suppl-4):s855-59.
23. Kukla P, Dudek D, Rakowski T, Dziewierz A, Mielecki W, Szczuka K, Dubiel JS. Inferior wall myocardial infarction with or without right ventricular involvement--treatment and in-hospital course. Kardiol Pol. 2006;64(6):583-8; discussion 589-90.

CONFLICT OF INTEREST: Authors declare no conflict of interest

GRANT SUPPORT AND FINANCIAL DISCLOSURE: NIL

AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under

Subhan S:	Conception and study design, acquisition of data, drafting the manuscript, critical review, approval of the final version to be published
Arafat Y:	Analysis and interpretation of data, drafting the manuscript, approval of the final version to be published
Khan JUA:	Acquisition of data, approval of the final version to be published
Jan H:	Critical review, approval of the final version to be published.
Qaisar A:	Critical review, approval of the final version to be published.
Shah AZ:	Drafting the manuscript, approval of the final version to be published

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

ORIGINAL ARTICLE

STABILITY OF ORTHODONTIC MINI-SCREWS AND DIFFERENT EXPERIENCE LEVELS OF RESIDENCY TRAINING OF STUDENTS

Palwasha Gul[1], Sana Ali[1], Ahsan Mehmood Shah[1], Humaira Saleem[1],Tahira Asghar[1], Farhad Ali[2]

[1]Department of Orthodontics and Dentofacial Orthopedics, Khyber College of Dentistry, Peshawar - Pakistan

[2]Epidemiology and Biostatistics, Khyber College of Dentistry, Peshawar - Pakistan

ABSTRACT

Objectives: To determine the association between the stability of orthodontic mini-screws with different experience levels of residency training of students.

Materials and methods: A total of 240 mini-screws with a diameter of 1.3 mm, and a length of 7 mm were inserted by orthodontic residents in the first, second, third, and fourth years. Stability was assessed after one month of application of orthodontic load. Chi-square tests were used to analyze data. P value ≤.05 was considered significant.

Results: Out of 240 implants, 172 were found to be stable and 68 were unstable after one month among different resident levels. There was a significant association between the stability of mini-screws and different experience levels of postgraduate residents. For first-year residents, stability was 53.8%, for second-year residents 27.3%, for the third year 93.3%, and the fourth year 90.5%. The association between the placement site of mini-screws and different levels of postgraduate residents was also significant and the highest number of stable mini-screws were found in maxilla and posterior mandible placed by fourth-year residents, and the least stable for second-year residents.

Conclusion: The experience level of residents is a significant factor in the stability of mini-screws and site-specific stability is higher in the maxilla and posterior mandible for fourth-year residents.

Key Words: Anchorage, Insertion site, Maxilla, Mandible, Orthodontists, Stability, Temporary Anchorage Devices (TADs).

This article may be cited as: Gul P, Ali S, Shah AM, Ali F, Saleem H, Asghar T. Stability of orthodontic mini-screws and different experience levels of residency. J Med Sci 2022 July;30(3):198-201

INTRODUCTION

The success of orthodontic treatment greatly depends on the anchorage control achieved.[1] Traditionally, for anchorage control, orthodontists use teeth, extra-oral means, or inter arch elastics. However, these methods require patients' compliance and it is difficult to achieve absolute anchorage using these means.[2,3]

Nowadays, orthodontists greatly opt for mini-screws for stationary anchorage.[4] Their high level of acceptance is because they are less technique sensitive and independent of compliance.[5] They are a source of absolute anchorage for retraction, protraction, and intrusion.[6-8] Lim et al. reported that experienced operators showed higher stability in mini-screw placement because of their knowledge and clinical experience. They were able to decide on an adequate angle for the insertion of mini-screws and maintain that angle during placement to avoid root injury, screw fracture, or any other complications.[9] Studies by Dobranszki and Moon also found that the stability of mini-screws has a significant relation to the operator's experience.[4,5] Regarding the site of placement and stability, a study by Topouzelis et al reported that screws in the posterior mandible and palate showed lower success rates as compared to the buccal site.[3]

The objective of our study is to find out whether in our setup the stability of the mini-screws is affected by residency level and site of placement in either jaw, as this may help us to predict which residency level requires more guidance and supervision, which may reduce the failure rate.

Correspondence
Dr. Ahsan Mehmood Shah
Chairman & Associate Professor
Department of Orthodontics and Dentofacial Orthopedics, Khyber College of Dentistry, Peshawar, Pakistan
Cell: +92-333-9117622
Email: ahsanmshah@gmail.com
Date Received: 22-04-2022
Date Revised: 09-09-2022
Date Accepted: 20-09-2022

MATERIALS AND METHODS

This cross-sectional study was conducted in the Department of Orthodontics, Khyber College of Dentistry, Peshawar from September 2020 to September 2021. Approval from the ethical committee was obtained in August 2020 (Ref. No. 12 ADR/KCD). A Convenient sampling technique was used for patient inclusion.

Orthodontic residents of all four years participated in the study. Year 1 had 12 first-year residents; Year 2 had 11 second-year residents; Year 3 had 12 third-year resi-

dents; Year 4 had 12 fourth-year residents. The residents eeveryyear had a different number of patients who already had been allotted to them for orthodontic treatment. These patients indicated mini-screws i.e. maximum anchorage cases.

Patients who had the following records were included in the study; date of insertion of the mini screw; diameter and length of the mini screw. Patients with systemic bone disorders and those on long-term medications were excluded.

The total number of patients was 90 (35 males and 55 females with a mean age of 20.62 years ± 4.29). The purpose, procedure, and associated risks and benefits of the study were explained to them. They were assured that the confidentiality of their data and records will be maintained. Informed consent was obtained from all participants.

The data of mini-screws inserted in patients was obtained from residents. A total of 240 titanium mini-screws of diameter 1.3 mm and a length of 7mm were inserted by residents over the four years. Year 1 inserted 52 mini-screws; Year 2 inserted 44; Year 3 inserted 60; Year 4 inserted 84 mini-screws.

The stability of mini-screws was observed concerning the level of residents and the site of placement after one month. The mini-screws were considered stable when there was an absence of pain and mobility. The pain was assessed after 24 hours and then 7 days after insertion, using a 10 points visual analog scale (VAS). Mobility was clinically assessed using cotton forceps by applying light force laterally to the head of the mini screw and if there was any detectable mobility, the mini screw was considered mobile and unstable; the scoring done was either 'stable' (immobile) or 'unstable' (mobile).[10]

Data obtained was analyzed by IBM SPSS version 25.0. Means and standard deviation for age, and frequency with percentages for the other categorical variables were calculated. Chi-square tests were done to check the association of experience level of residents and site of placement with the stability of mini-screws. A p-value of ≤ 0.05 was considered significant.

RESULTS

Of the total 47 orthodontic residents, 17 were males and 30 were females. The mean age of the residents included in the study was 25 years ± 1.28.

The overall percentage of stable mini-screws after a period of one month was 71% and that of unstable mini-screws was 28%.

Of the total stable mini-screws, the highest percentage was found in Year 3 (93.3%) and the lowest percentage in Year 2 (27.3%). Results were statistically significant (p-value <.001) for the different Years (Table-1).

Based on the site of placement, the highest number of stable mini-screws was found in Year 4 in the anterior maxilla (100%) and posterior mandible (100%), followed by the posterior maxilla (93.8%).

These results were statistically significant with p <.001. The highest number of unstable mini-screws was found in Year 2 in the posterior maxilla (57.1%) and posterior mandible (100%), with p=.002. For the other two years, the results regarding site-specific stability were insignificant.

Table 1: Chi-square test for stability of mini-screws among the four Years after 1-month duration.

Residency Year	Stable after 1 month		Unstable after 1 month		P value
	N	%	n	%	
Year 1	28	53.8%	24	46.2%	.000
Year 2	12	27.3%	32	72.7%	
Year 3	56	93.3%	4	6.7%	
Year 4	76	90.5%	8	9.5%	

Table 2: Stability of mini screw in Year 1 according to the site of placement.

	Stable after 1 month		Unstable after 1 month		Chi square test	P value
	N	%	n	%		
Ant. Maxilla	-	-	-	-	0.05	.812
Post. Maxilla	24	54.5	20	45.5		
Ant. Mandible	-	-	-	-		
Post. Mandible	4	50	4	50		

Table 3: Stability of mini-screws in Year 2 according to the site of placement.

	Stable after 1 month		Unstable after 1 month		Chi square test	P value
	N	%	n	%		
Ant. Maxilla	-	-	-	-	9.42	.002
Post. Maxilla	12	42.9	16	57.1		
Ant. Mandible	-	-	-	-		
Post. Mandible	0	0	16	100		

n= number of screws

%= Percentage of screws for that site of placement

Post= posterior

Ant= anterior

Table 4: Stability of mini-screws in Year 3 according to the site of placement.

	Stable after 1 month		Unstable after 1 month		Chi square test	P value
	N	%	n	%		
Ant. Maxilla	4	100	0	0	2.14	.343
Post. Maxilla	36	90	4	10		
Ant. Mandible	16	100	0	0		
Post. Mandible	-	-	-	-		

n= number of screws

%= Percentage of screws for that site of placement

Post= posterior

Ant= anterior

Table 5: Stability of mini-screws in Year 4 according to the site of placement.

	Stable after 1 month		Unstable after 1 month		Chi square test	P value
	N	%	n	%		
Ant. Maxilla	8	100	0	0	40.48	.000
Post. Maxilla	30	93.8	4	6.2		
Ant. Mandible	0	0	4	100		
Post. Mandible	8	100	0	0		

n= number of screws

%= Percentage of screws for that site of placement

Post= posterior

Ant= anterior

DISCUSSION

In our study, the experience level of the residents and the site of placement were the two factors evaluated for the stability of mini-screws after 1 month of insertion.

When considering the experience of the operator, the highest number of stable mini-screws were found for final-year residents and the lowest for second-year residents.

The number of stable mini-screws inserted by first-year residents was also more than that of second-year residents. This may be due to the reason that first-year residents insert mini-screws in their presence and under the guidance of their teachers, whereas, second-year residents prefer to perform mini-screw insertions independently. Then, with increasing experience in performing independent mini screw insertions, the stability increases over the years, from the second year to the final year.

Similar to our study, in a study by Choa et al on root contact during drilling for micro implant placement, it was concluded that operator experience was an important factor.[11] The operator might experience a high number of micro implant failures due to root contact in the initial period but this risk is markedly lowered in subsequent years as they gain experience in the field.

In another study by Lim et al., it was concluded that the experience of the operator is an important factor in the stability of mini-screws.[9] The authors reported that the mini-screws inserted by more experienced operators had 3.6 times higher initial stability as compared to those inserted by less experienced operators.

On the contrary, Moon et al in their study concluded that success rate is not affected by operator experi-

ence.[5] In our study, the site-specific stability was higher in the maxilla and posterior mandible ($p<.001$) for final-year residents. Jing et al reported that the site of placement is a significant factor in the success rate of mini-screws, and the stability of the mini-screws inserted in the maxilla is more than that of the mandible.[12] On the contrary, a study by Song Yi Lin et al showed that there is no significant association between the success rate of mini-screws and their site of insertion. [13] Our study did not address a few confounding factors, such as the age and gender of the patients, different lengths and diameters of screws, and the directions of force applied on the mini-screws, which may influence the failure rate.[4] Only the site of placement and operator experience were evaluated using a single type of mini screw. Further studies regarding the effects of these possible confounding factors should be carried out.

CONCLUSION

With increasing experience in performing independent mini screw insertions, the stability of mini-screws increases over the years, from the second year to the final year. Site-specific stability is higher in the maxilla and the posterior mandible for final-year residents.

REFERENCES

1. Park H, Jeong S, Kwon O. Factors affecting the clinical success of screw implants used as orthodontic anchorage. Am J Orthod Dentofacial Orthop.2006;130(1):18-25. https://doi.org/10.1016/j.ajodo.2004.11.032
2. Yi Lin S, Mimi Y, Ming Tak C, Kelvin Weng Chiong F, Hung Chew W. A Study of Success Rate of Miniscrew Implants as Temporary Anchorage Devices in Singapore. Int J Dent.2015; Mar 2015:1-10. https://doi.org/10.1155/2015/294670
3. Topouzelis N, Tsaousoglou P. Clinical factors correlated with the success rate of miniscrews in orthodontic treatment. Int J Oral Sci. 2012 Jan;4(1):38-44. https://doi.org/10.1038/ijos.2012.1
4. Dobranszki A, Faber J, Scatolino I, Dobranszki N, Toledo O. Analysis of Factors Associated with Orthodontic Microscrew Failure. Bra Dent J. 2014;25(4):346-51. http://doi.org/10.1590/0103-6440201300125
5. Moon C, Park H, Nam J, Im J, Baek S. Relationship between vertical skeletal pattern and success rate of orthodontic mini-implants. Am J Orthod Dentofacial Orthop. 2010 Jul 14;138(1):51-57. http://doi.org/10.1016/j.ajodo.2008.08.032
6. Kuroda S, Tanaka E. Risks and complications of miniscrew anchorage in clinical orthodontics. Jpn Dent Sci Rev.2014;50(4):79-85. http://doi.org/10.1016/j.jdsr.2014.05.001
7. Manni A, Cozzani M, Tamborrino F, De Rinaldis S, Menini A. Factors influencing the stability of miniscrews. A retrospective study on 300 miniscrews. Eur J Orthod. 2010 Oct 12;33(4):388-395. https://doi.org/10.1093/ejo/cjq090
8. Giuliano Maino B, Pagin P, Di Blasio A. Success of mini-screws used as anchorage for orthodontic treatment: analysis of different factors. Prog Orthod. 2012 Nov 1;13(3):202-209. https://doi.org/10.1016/j.pio.2012.04.002
9. Lim H, Choi Y, Evans C, Hwang H. Predictors of initial stability of orthodontic mini screw implants. Eur J Orthod. 2011 Jan 14;33(5):528-532. https://doi.org/10.1093/ejo/cjq122
10. Intachai I, Krisanaerakornkit S, Kongtawelert P, Ong-Chai S, Buranastidporn B, Suzuki EY, Jotkasthira D. Chondroitin sulphate (WF6 epitope) levels in peri-miniscrew implant crevicular fluid during orthodontic loading. Eur J Orthod. 2010 Feb 1;32(1):60-5. https://doi.org/10.1093/ejo/cjp056
11. Cho U, Yu W, Kyung H. Root Contact during Drilling for Micro implant Placement. Angle Orthod. 2010;80(1):130-136. https://doi.org/10.2319/011509-535.1
12. Jing Z, Wu MSY, Jiang W, Zhao L, Jing D. Factors Affecting the Clinical Success Rate of Miniscrew Implants for Orthodontic treatment. Int J Oral Maxillofac Implants. 2016 Jul-Aug;31(4):835–41. https://doi.org/10.11607/jomi.4197
13. Lin SY, Mimi Y, Tak CM, Kelvin F, Chiong W, Chew WH. A Study of Success Rate of Miniscrew Implants as Temporary Anchorage Devices in Singapore. Int J Dent. 2015;2015:294670. https://doi.org/10.1155/2015/294670

CONFLICT OF INTEREST: Authors declare no conflict of interest

GRANT SUPPORT AND FINANCIAL DISCLOSURE: NIL

AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under

Gul P:	Conception, literature search and overall supervision
Ali S:	Writing up
Shah AM:	Data collection
Ali F:	Statistical analysis
Saleem H:	Bibliography
Asghar T:	Data collection

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

ORIGINAL ARTICLE

OUTCOMES OF WHIPPLE PROCEDURE FOR PANCREATIC CANCER: INITIAL EXPERIENCE FROM A PUBLIC-SECTOR HOSPITAL OF PAKISTAN

Syed Ali Haider, Wardah Jabeen, Raza Haider, Amsa Zafar, Syeda Sarah Kazmi

Dow Medical College and Dr. Ruth K. M. Pfau Civil Hospital, Karachi - Pakistan

ABSTRACT

Objectives: The objective of this study was to review the outcomes of Whipple procedure at our institution.

Material and methods: From 1st January 2017 to 31st December 2019, patients who underwent Whipple procedure for pancreatic cancer at Dr. Ruth K.M. Pfau Civil Hospital Karachi complying with the criteria were chosen for this retrospective cross-sectional study utilizing convenient sampling. Ages, gender, site of the disease, histopathology, operative findings, pancreatic reconstruction techniques, postoperative complications including SSI, intra-abdominal collections, chyle leaks, anastomotic leaks, and their management and 30-day mortality were recorded and analyzed.

Results: The mean age of patients was 57±13.62 years. The male-to-female ratio was 2.1:1. Jaundice was the most common symptom patients encountered. Surgical site infection (SSI) was the leading postoperative complication. Metastasis to distant sites or locoregional recurrence evolved in 32.7% of patients. The 30-day mortality after surgery was 17.07%. 27 patients (65.9%) of the patients are alive and disease free and 14 patients (34.1%) expired due to recurrence.

Conclusion: Pancreaticoduodenectomy is a complex procedure. However, with recent advancements, it has evolved into a safer procedure with significantly better surgical outcomes. Large-scale studies for identifying factors priming in poor outcomes along with stage-based and age-based comparisons are recommended.

Keywords: Whipple procedure, Pancreatogastrostomy, Pancreatojejunostomy, outcome, Survival

This article may be cited as: Haider SA, Jabeen W, Haider R, Zafar A, Kazmi SS. Outcomes of whipple procedure for pancreatic cancer. initial experience from a public-sector hospital of Pakistan. J Med Sci 2022 July;30(3):202-206

INTRODUCTION

Among the leading malignant diseases causing deaths around the globe, pancreatic cancer stands at the 7th spot worldwide [1]. There are two main types of pancreatic cancers i.e., adenocarcinoma and pancreatic endocrine tumors [1,2]. The incidence of pancreatic cancer increases with advancing age and is slightly more common among the female gender[3]. The cause of pancreatic cancer is still unknown, however, some risk factors have been identified in the past few decades such as; age, gender, race, alcohol, smoking, obesity, family history, and diabetes [4]. It has dreadful prognostic statistics with a 5-year survival rate ranging from 2% to 9%[5].

Surgery, alongside chemotherapeutic options, remains an elemental component of the management plan. Pancreaticoduodenectomy (Whipple procedure) is a complex surgical undertaking and has a noteworthy morbidity rate associated with it. History credits Walter Kausch as the debutante for doing the initial Whipple procedure successfully, which he performed in stages. But the procedure secured its name as Whipple's procedure after Allan Oldfather Whipple publicized it for periampullary tumors in his publication in the year 1935. Back in Sir Whipple's days and as per his published case series, the postprocedural mortality was hefty, estimated to be 25 percent[6]. In recent times, high-volume centers have communicated a significant reduction in mortality rates, in some reports less than 5% crediting furtherance in surgical art, periprocedural care, and intensive care facilities. Nonetheless, morbidity rates still peak at 40 to 50 percent calling for apt strategies[7].

The indications of Whipple procedure include malignant pancreatic and periampullary tumors and some benign conditions including chronic pancreatitis and pancreatic trauma. Pancreatic head adenocarcinoma carries a dismal prognosis as compared to periampullary tumors. Most of the patients at presentation have advanced stages of the disease, and only 10% to 20% of them have operable tumors [8].

Several authors from Pakistan have published their experience regarding the outcomes of Whipple pro-

Correspondence
Dr. Syed Ali Haider
Assistant Professor
Department of Surgery, Dow Medical College &
DR Ruth K M Pfau Civil Hospital, Karachi - Pakistan
Cell: +92-321-8203820
Email: dralihaider@gmail.com
Date Received: 24-05-2022
Date Revised: 20-09-2022
Date Accepted: 22-09-2022

cedure from tertiary care centers but the numbers have been small[9]. The goal of this study was to examine the outcomes in terms of postoperative morbidity and 30-day mortality while additionally reviewing the clinical and pathological features of Whipple procedure at our institution. This will aid in scaling the exact statistical picture of the morbidity and mortality risk to the patients undergoing this complex procedure in local patients.

MATERIAL AND METHODS

From 1st January 2017 to 31st December 2019, patients who underwent Whipple procedure for pancreatic cancer at Dr. Ruth K.M. Pfau Civil Hospital Karachi were sought for this retrospective cross-sectional study employing convenient sampling. Patients having known metastatic disease at presentation and having celiac artery, superior mesenteric artery, or hepatic artery involved/invaded on scans done before the procedure were excluded. The investigators started data collection after procuring approval from the Institutional Review Board (IRB) of Dr. Ruth K.M. Pfau Civil Hospital.

A detailed history of selected patients planned to undergo Whipple procedure, obtained and recorded in the database and relevant investigation results namely liver functions, coagulation profile, CA 19-9, and endoscopic retrograde cholangiopancreatography were sought. Staging workup of the selected patients included triphasic CT scan abdomen and contrast-enhanced CT chest (CECT).

Data was collected through the database of Dr. Ruth K.M. Pfau Civil Hospital Karachi. Recording of variables concerning the demographic qualities and clinical variables like histopathology if done before definitive operations, clinical stages, per operative findings, the type of pancreatic anastomosis constructed, complications that developed after surgeries including SSI, abdominal collections, anastomotic leaks, chyle leaks, recurrence, was done. The specific anastomosis that developed leaks, the site of recurrence, whether anastomotic or far-site organ, and early mortality occurring within 30 days of procedure were also taken into the record. The management measures are taken, and outcome weighed in terms of survival were recorded.

Statistical Package for the Social Sciences (SPSS 20) software was put to use to explore and analyze the collected data. Statistical derivation of means, standard deviations of ages of the patients, median survival, and descriptive details of qualitative variables was conducted using the aforementioned software.

RESULTS

In our setup 41 patients had Whipple procedure from 1st January 2017 to 31st December 2019, of which twenty-eight patients were males whereas female patients were thirteen in number. The median age in our institution was 57 (30-78) years. None of the patients received neoadjuvant chemotherapy. Jaundice was the most common symptom patients encountered in 83% of patients followed by abdominal pain in 12%. Table 1 further details the demographics and oncological statuses, stage, choice of pancreatic anastomotic reconstruction, and early mortality of the patients.

Surgical site infection (SSI) was developed in 15 patients, whereby the Southampton wound scoring system was employed to identify superficial and deep SSI. Grades 2, 3 & 4 were labeled superficial SSI on the other hand wounds complying with Southampton Grade 5 were accounted for Deep SSI (Table 2)

8 patients had PG leak, 2 had PJ leak and 1 had hepaticojejunostomy (HJ) leak. Re-look laparotomy was performed in 11 patients for anastomotic leak management. 5 patients with PG leak were managed by taking down the anastomosis and constructing a PJ after debriding the distal stump of the pancreas while doing anastomosis was precluded by extensive inflammation and edema in the rest of the 3 cases, requiring ligation of the pancreatic stump. One PJ leak was negotiated by debriding the pancreatic stump, refreshing the jejunal margins, and fashioning an invaginating pancreatic anastomosis while the other PJ leak required distal pancreatectomy owing to extensive pancreatic inflammation and necrosis. The patient with HJ leak only required oversewing of the minor leak and drain placement. Intra-abdominal drain placement was performed in 6 patients (Table 2).

Distant metastases or locoregional recurrence evolved in 32.7 % of the patients (Table 2). Some of the patients had both local recurrences as well as metastasis after treatment. 27 patients (65.9%) are alive and disease free and 14 patients (34.1%) died. Median overall survival is 28±14.5 months (Figure 1).

DISCUSSION

Whipple's Whipple procedure is still an overly onerous surgical undertaking requiring high dexterity and carries a significantly high rate of postprocedural complication and mortality [10]. Advancement has improved the outcomes, but morbidity and mortality remain beyond 50% and 2% respectively [11]. However, with improved and comparably early diagnosis, betterment in operative techniques, and biomedical and intensive care facilities furtherance, the world is seeing more Whipple procedures performed for both benign and malignant diseases in recent times.

This retrospective study showed that the mean age of patients was 57 years, ranging from 30-78 years which is lower than other published literature [12,13]. The majority of the patients were males comprising sixty-eight percent.

Surgery is the most important component in the

Table 1: Demographics and Oncological Characteristics.

VARIABLES	Frequency (%)
Gender	
Male	28 (68.3%)
Female	13 (31.7%)
Age (years)	
Pathology	
Well-differentiated adenocarcinoma	3 (7.3%)
Moderately differentiated adeno-carcinoma	33 (80.5%)
Poorly differentiated carcinoma	5 (12.2%)
Stage of disease	
Stage 1	18 (43.9%)
Stage 2	14 (34.1%)
Stage 3	9 (22.0%)
Site of Disease	
Pancreatic head	26 (63.4%)
Ampullary	14 (34.1%)
Uncinate process	1 (2.4%)
Reconstruction technique	
Pancreatojejunostomy	7 (17.1%)
Pancreaticogastrostomy	34 (82.9%)
30-day Mortality	7 (17.07%)
Median overall survival (months)	28±14.5

Table 2: Complications.

Variables	Frequency (%)
Superficial SSI	11 (26.82%)
Deep SSI	4 (9.75%)
Anastomotic leak	11 (26.82%)
Intra-abdominal collection	11 (26.82%)
Chyle leak	3 (7.3%)
Recurrence	
Liver	4 (9.75%)
Lungs	2 (4.88%)
Loco-regional	4 (9.75%)
Anastomotic site recurrence	1 (2.43%)

management of pancreatic cancer. However, due to the advanced nature of the disease and lack of advanced facilities in the country, most of the patients presented with the late disease either Stage III or IV disease.

There is a perennial discourse amongst professionals regarding the technique for reconstructing the pancreatoenteric continuity, where in the literature some surgeons communicated PG as the better of the two while others found no difference with PJ statistically in terms of outcome [14-16]. 8 (23.5%) PG/anastomotic leaks developed in 34 patients who were reconstructed with pancreatogastric anastomosis while 2 of the 7 PJ reconstructions developed anastomotic leaks in our institute during the selected study period.

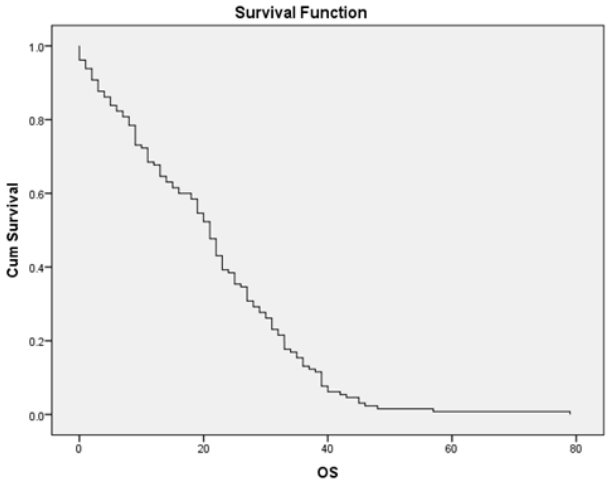

Fig 1: Over-all survival of patients undergone Whipple procedure for pancreatic cancer

The rate of SSI in this research was comparable to other published literature which was 36.5%. Literature from the USA, the reported rate of SSI ranged from 15 to 27% [17-19]. A study from Iraq reported a higher rate of SSI (23.5%)[20].

In our study, twenty-six percent of patients developed intra-abdominal collection following surgery which is comparable[19, 21, 22]. However, none of the patients needed re-exploration for the above-mentioned complications, six patients had drain placement with help of interventional radiology.

The rate of anastomotic leak in our study was 26.82% which is comparable to others. The risk factors of anastomotic leak after Whipple procedure are the same as that of other anastomoses. Pancreatic texture and technique of anastomosis are determining factors of the risk of Postoperative pancreatic Fistula (POPF) development. The risk of POPF is elevated in patients having a small diameter/nondilated main pancreatic duct and soft pancreas [23, 24].

The 30-day mortality following Whipple procedure in our patients was 17.07%. The reported mortality in literature is less than five percent [10, 22, 25-27]. However, the recurrence was seen in 32% of the patients. Liver and lymph node involvement were the commonest sites of recurrence.

Although this study gives insight into the clinical details, stage distribution, post-surgical complications, and early mortality of local patients who underwent Whipple procedure in a public sector tertiary care Centre, the retrospective nature of this study is the limitation of the study. The study did not compare the outcomes of dif-

ferent surgical techniques. A comparison of stage and age-related outcomes of Whipple procedure was also not performed.

CONCLUSION

Pancreaticoduodenectomy is a complex procedure. However, with recent advancements, it has evolved into a safer procedure with significantly better surgical outcomes. Authors recommend consistent publishing of data from all surgical facilities performing Whipple's Whipple procedure for identification of complications, collective learning, and furtherance for better outcomes.

REFERENCES

1. Rawla P, Sunkara T, Gaduputi V. Epidemiology of Pancreatic Cancer: Global Trends, Etiology and Risk Factors. World J Oncol. 2019;10(1):10-27.
2. McGuigan A, Kelly P, Turkington RC, Jones C, Coleman HG, McCain RS. Pancreatic cancer: A review of clinical diagnosis, epidemiology, treatment, and outcomes. World J Gastroenterol. 2018;24(43):4846-4861.
3. Capasso M, Franceschi M, Rodriguez-Castro KI, Crafa P, Cambiè G, Miraglia C, et al. Epidemiology and risk factors of pancreatic cancer. Acta Biomed. 2018;89(9-S):141-146.
4. Olakowski M, Bułdak Ł. Modifiable and Non-Modifiable Risk Factors for the Development of Non-Hereditary Pancreatic Cancer. Medicina (Kaunas). 2022;58(8):978.
5. Hu JX, Zhao CF, Chen WB, Liu QC, Li QW, Lin YY, et al. Pancreatic cancer: A review of epidemiology, trend, and risk factors. World J Gastroenterol. 2021;27(27):4298-4321.
6. Whipple AO. Present-day surgery of the pancreas. New England J Medicine. 1942;226(13):515-26.
7. Kumar SV, Prasad JS. A Postoperative morbidity following Whipple's procedure for periampullary carcinoma: a retrospective study spanning 5 years. Int J Res Med Sci 2019;7:4314-9.
8. De Luca L, Repici A, Koçollari A, Auriemma F, Bianchetti M, Mangiavillano B. Pancreatoscopy: An update. World J Gastrointest Endosc. 2019;11(1):22-30.
9. Bari H, Chawla T, Effendi S. Pancreaticogastrostomy–An alternate for dealing with pancreatic remnant after pancreaticoduodenectomy–Experience from a tertiary care center of Pakistan. HPB. 2018;20:S588.
10. Changazi SH, Ahmed Q, Bhatti S, Siddique S, Abdul Raffay E, Farooka MW, et al. Whipple Procedure: A Five-Year Clinical Experience in Tertiary Care Center. Cureus. 2020;12(11):e11466.
11. De Pastena M, Paiella S, Marchegiani G, Malleo G, Ciprani D, Gasparini C, et al. Postoperative infections represent a major determinant of outcome after pancreaticoduodenectomy: results from a high-volume center. Surgery. 2017;162(4):792-801.
12. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2018;68(6):394–424.
13. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2018. CA Cancer J Clin. 2018;68(1):7–30.
14. Hackert T, Büchler M. Randomized clinical trial of isolated Roux-en-Y versus conventional reconstruction after pancreaticoduodenectomy.). Br J Surg. 2014;101:1092.
15. Lee JY, Kim EY, Lee JS, Lee SH, Na GH, Hong TH, et al. A novel pancreaticogastrostomy method using only two transpancreatic sutures: early postoperative surgical results compared with conventional pancreaticojejunostomy. Annals of surgical treatment and research. 2015;88(6):299-305.
16. Anwer AW, Khattak S, Yusuf MA, Syed AA, Hanif F. Surgical outcome of pancreaticoduodenectomy in pancreatic and periampullary neoplasms. J College of Physicians and Surgeons Pakistan. 2017;27(9):559-62.
17. Cengiz TB, Jarrar A, Power C, Joyce D, Anzlovar N, Morris-Stiff G. Antimicrobial Stewardship Reduces Surgical Site Infection Rate, as well as Number and Severity of Pancreatic Fistulae after Pancreatoduodenectomy. Surg Infect (Larchmt). 2020;21(3):212-217.
18. Padussis JC, Zani S, Blazer DG, Tyler DS, Pappas TN, Scarborough JE. Feeding jejunostomy during Whipple is associated with increased morbidity. J surgical research. 2014;187(2):361-6.
19. Fernández-del Castillo C, Morales-Oyarvide V, McGrath D, Wargo JA, Ferrone CR, Thayer SP, et al. Evolution of the Whipple procedure at the Massachusetts General Hospital. Surgery. 2012;152(3):S56-S63.
20. Karim SAM, Abdulla KS, Abdulkarim QH, Rahim FH. The outcomes and complications of pancreaticoduodenectomy (Whipple procedure): Cross sectional study. Intern J Surgery. 2018;52:383-7.
21. Bell RH. Pancreaticoduodenectomy with or without pylorus preservation have similar outcomes: Abstracted from: Tran KTC, Smeenk HG, van Eijck CHJ, et al. Pylorus preserving pancreaticoduodenectomy versus standard Whipple procedure–a prospective, randomized, multicenter analysis of 170 patients with pancreatic and periampullary tumors. Ann Surg 2004; 240: 738–45. Cancer treatment reviews. 2005;31(4):328-31.
22. Ujiki MB, Talamonti MS, editors. Surgical management of pancreatic cancer. Seminars in radiation oncology; 2005: Elsevier.
23. Elberm H, Ravikumar R, Sabin C, Hilal MA, Al-Hilli A, Aroori S, et al. Outcome after pancreaticoduodenec-

tomy for T3 adenocarcinoma: a multivariable analysis from the UK Vascular Resection for Pancreatic Cancer Study Group. European J Surgical Oncology (EJSO). 2015;41(11):1500-7.

24. Yardimci S, Kara YB, Tuney D, Attaallah W, Ugurlu MU, Dulundu E, et al. A simple method to evaluate whether pancreas texture can be used to predict pancreatic fistula risk after pancreatoduodenectomy. J Gastrointestinal Surgery. 2015;19(9):1625-31.

25. Jakhmola C, Kumar A. Whipple's pancreaticoduodenectomy: Outcomes at a tertiary care hospital. medical journal armed forces india. 2014;70(4):321-6.

26. Prenzel KL, Hölscher AH, Grabolle I, Fetzner U, Kleinert R, Gutschow CA, et al. Impact of duct-to-mucosa pancreaticojejunostomy with external drainage of the pancreatic duct after pancreaticoduodenectomy. Journal of Surgical Research. 2011;171(2):558-62.

27. Cameron JL. One thousand consecutive pancreaticoduodenectomies and beyond: a personal series. American J surgery. 2007;194(4):S11-S5.

CONFLICT OF INTEREST: Authors declare no conflict of interest

GRANT SUPPORT AND FINANCIAL DISCLOSURE: NIL

AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under

Haider SA: Conceiving and designing the study, col lection, analysis, interpretation of data, Manuscript writing, Approval of Final draft

Jabeen W: Conceiving and designing the study, collection of data, drafting, Approval of Final draft

Haider R: Collection of data, analysis, interpretation of data, drafting

Zafar A: Collection of data, drafting, Manuscript writing

Kazmi SS: Collection of data, drafting, Manuscript writing

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

ORIGINAL ARTICLE

EXPLORING STUDY HABITS OF MEDICAL STUDENTS IN AN UNDERGRADUATE MEDICAL SCHOOL IN PESHAWAR: A DESCRIPTIVE CROSS-SECTIONAL STUDY

Haya Mushtaq

2nd-year medical student, Khyber Medical College, Peshawar - Pakistan

ABSTRACT

Objectives: To explore the study habits of undergraduate medical students and their study schedule strategies.

Material and Methods: This was a cross-sectional study conducted on medical students at Khyber Medical College, Peshawar, in May 2019. A total of 118 students were invited to participate in the survey using the convenience sampling technique. However, 82 (69%) students returned signed consent forms and were then asked to complete the questionnaire. All respondents provided information about their study schedules and routines.

Results: Most of the students who scored between 80 and 90% in their academics tended to study for about 2-4 hours a day, could concentrate for 1-2 hours at a stretch, and switched places during their studies. Students scoring above 90% reported studying from 9 to more than 12 hours daily, studying from 2 to more than 3 hours in one stretch, and their studies were unaffected by vacations.

Conclusion: The students achieving higher academic scores studied regularly for about 2-4 hours daily, could concentrate for 1-2 hours at a stretch, preferred switching places during their studies, and took breaks that lasted around 30 minutes.

Key Words: medical students, study skills, academic performance.

This article may be cited as: Mushtaq H. Exploring study habits of medical students in an undergraduate medical school in Peshawar: a descriptive cross-sectional study. J Med Sci 2022 July;30(3):207-211

INTRODUCTION

Studying medicine can be challenging. Only the best students from high schools and pre-medical studies get into medical schools after passing through a thorough selection process.[1] The medical field can get extremely stressful and tough, which ultimately leads to a fall in academic performance. Students in medical schools face numerous obstacles because of the vast amount of knowledge, and so, even students who have previously excelled academically may need to develop new study strategies.[2] Academic performance and achievements both within and outside of the classroom are determined by effectual study techniques.[3]

Developing effective study approaches is crucial to academic achievement and plays a significant role in medical school achievement. Since students in medical training are adult learners, they are required to use effective methods to accomplish their goals.[4] Often, new college students lack the necessary skills to handle the difficulties of the different learning environments. Their flexibility to adopt the best tactics for a specific learning circumstance will ultimately determine whether they are successful or unsuccessful in their curriculum. [5] A variety of coordinated cognitive abilities and practices that improve students' learning efficacy are referred to as study skills. [6]

Research on the individual study strategies of successful medical students is lacking. This study sought to explore the study schedule strategies that academically successful students make use of, with successful students being defined as those who scored 80% or more on their last professional examination. In particular, we were interested in how these students manage their time efficiently and how they time their study routine. Sharing the results of this study may help future students to guide them in enhancing their learning strategies.

MATERIALS AND METHODS

Khyber Medical College (KMC), Peshawar, has been a pioneer institution in medical education in Khyber Pakhtunkhwa (KP) since 1954. Today, KMC enrolls about 250 students yearly, and a large number of graduates who pass out from KMC are providing healthcare, not only in KP and its merged districts but also in the rest of the country and even abroad. The participants of this study were Year 3 medical students at KMC, who were included in

Correspondence
Haya Mushtaq
2nd-year medical student, Khyber Medical College, Peshawar - Pakistan
Cell: +92-302-1126464
Email: hayamushtaq29@gmail.com
Date Received: 27-06-2022
Date Revised: 11-08-2022
Date Accepted: 30-08-2022

the study using the non-probability convenience sampling technique. The research was based on a simple descriptive cross-sectional survey design.

A structured questionnaire that was used in this research consisted of two sections. The first section had 3 questions, which were designed to collect the demographic data of the respondents. The second section consisted of 11 questions and required the students to first give the results for their previous professional examinations and then go on to particular questions like how many study hours their day consisted of, how long they studied in one stretch, etc. The questionnaire was pilot tested on Year 4 students at KMC. Those questions that had ambiguities were refined by the field experts. The questionnaire was then distributed among Year 3 medical students at KMC to collect information on how they manage time for their academic activities. A total of 118 students present at the time of the distribution of the questionnaire were invited to participate in the survey. However, 82 students returned signed consent forms and were then asked to complete the questionnaire. All the students remained anonymous during the data collection.

Once the data was collected, it was analyzed using SPSS-22. Participants self-reported performance in the last year (exhibited in the form of marks obtained; i.e., 60-70%, 70-80%, 80-90%, and above 90%) was used to place students in one of four groups. Successful students were those who scored 80% to 90% or more than 90%. Frequencies of students' study habits; study hours in a day; making use of schedule making; studying in one stretch, etc., were reported for the entire group and separately divided into categories based on average scores during their most recent year of medical school. Incomplete questionnaires were excluded from the analysis.

RESULTS

Data was collected from a total of 82 third-year medical students of KMC, which comprised 61% (n = 50) male and 39% (n = 32) female respondents. Results are shown in Table 1.

In terms of study habits, Figure 1 shows the comparison between hours studied and marks obtained by the students, while Figure 2 shows study duration (in one stretch) and marks obtained by the students.

More than 12 hours of the study was not strongly associated with success, as only 1 student scoring above 90% reported doing so, and none of the students who had made between 80-90% fell into that category, as shown in figure 1.

Analysis showed that studying for a very long time in one stretch does not always result in academic success, as shown in figure 2. Students who had scored between 80 and 90% were found to have studied for only about 1-2 hours in one stretch. Studying for more than 3 hours in one stretch was not associated with success, as only 1 student who had scored above 90% reported doing so.

Two of the students who had scored above 90% reported having the same concentration level even during vacations. On the other hand, 7 (58.3%), i.e., the majority of those who had scored between 80-90%, stated that they studied only if they had an examination approaching after the vacations. This is in contrast to the students who had scored between 70 and 80%, as 19 (35%) students claimed that their concentration level was not like the other working days or, to be precise, they did not study like regular days during vacations.

The data regarding the duration of breaks for successful students and regular students demonstrated interesting trends. It was observed that 1 of the students who had scored above 90% took study breaks lasting less than 30 minutes, while another reported his study breaks lasted between 30 minutes and 1 hour. Similarly, 10 (83.3%) students who had scored between 80 and 90% reported that their study breaks lasted between 30 minutes and 1 hour. Many of the students, i.e., 13 (24%) who had scored between 70-80%, stated that they took breaks of more than 2 hours in length. In the same manner, 3 (29%) students who had scored between 60 and 75% fell under the same category.

The results also demonstrated that switching places during the study might be beneficial. Half of the students who had scored above 90% reported changing places during the study. In the same way, 8 (67%) students between 80-90% also fell into the same category. On the contrary, 24 (44%) students who had scores between 70 and 80% said they did not switch places during studying. The same was the case with the students who fell into the 60–70% group.

Other than the study schedule strategies used by successful students, some other random trends were also observed in the data. There was a significant statistical association between the scores of hostellers and day scholars. Those students who had scored above 90% had 1 (50%) hosteller and 1 (50%) day scholar. Those who had scored between 80-90% consisted of 9 (75%), i.e., the majority of day scholars, while only 3 (25%) were hostellers. On the contrary, the majority of those students who had scored between 60 and 70% were hostellers, i.e., 11 (79%), and the same was the case with the students who had scored between 70 and 80%.

DISCUSSION

The results indicated that some study strategies were linked to success in medical school. One important finding of the analysis was that studying for longer periods does not always lead to academic success. Results indicated that most of those students who performed well

Table 1: Questionnaire along with the responses received.

PARTICIPANT'S DEMOGRAPHIC DATA:				
No. of Participants	82			
Mean age (standard deviation):	21.35 (SD: 0.89)			
Gender (in percentages)	Male: 61%, Female: 39%			
SURVEY QUESTIONS				
1. Academic result in previous professional examination:	60-70%	70-80%	80-90%	Above 90%
Respondents	14	54	12	2
2. Are you a:	Hosteller/ Boarders		Day scholar	
Respondents	53		29	
3. Do you have a study schedule?	Yes		No	
Respondents	28		54	
4. What is your optimal time of the day for studying?	Morning hours		Evening hours	
Respondents	32		50	
5. How much do you tend to study with concentration in one stretch?	30-45 minutes	1-2 hours	2-3 hours	More than 3 hours
Respondents	34	35	9	4
6. How long does your study break last?	5-15 minutes	15-45 minutes	1-2 hours	More than 2 hours
Respondents	14	37	12	19
7. How many study hours does your day consist of?	2-4 hours	4-9 hours	9-12 hours	More than 12 hours
Respondents	52	22	6	2
8. Do you study more on:	Weekends		Weekdays	Equally on both
Respondents	43		18	21
9. Do you study with complete concentration even during vacations?	Depends on when my next examination is		Yes	No
Respondents	26		31	25
10. Does your study capacity and concentration level die down over the week?	Sometimes		Yes	No
Respondents	16		52	14
11. Do you switch places during your study?	Yes		No	
Respondents	47		35	

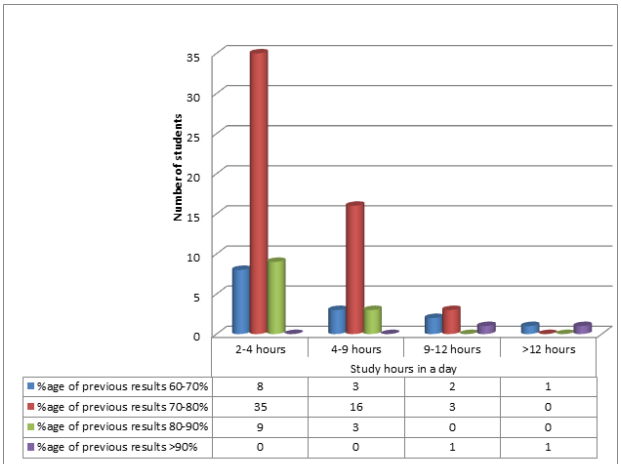

Fig 1: Comparison between hours studied per day and individual scores obtained.

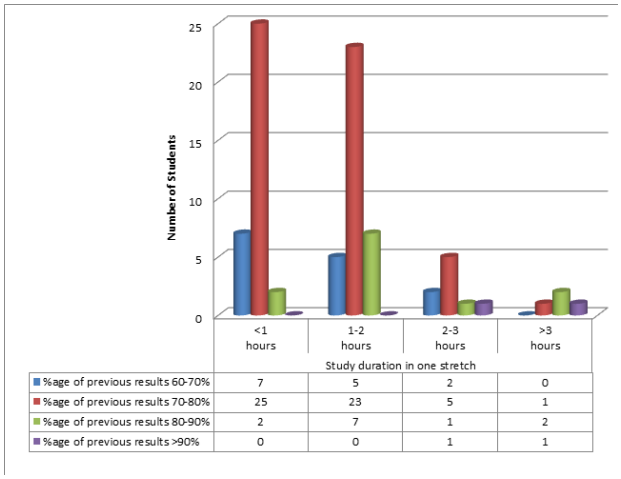

Fig 2: Study duration in one stretch vs. individual score obtained.

on examinations (i.e., scored between 80-90%) studied for about 2-4 hours a day. The results of our study were similar to another study, which stated that the most successful students overall were the ones studying for about 6–8 hours a day outside the classroom. [2] Of note, only 2 students who had scored above 90% said that they studied for more than 9 hours daily. This showed that it is better not to study for longer periods while giving up on other activities. These results were in contrast to another study, which stated that significantly higher scores were associated with more than 15 hours of study per day. [7]

Another observation made was to divide study time across short, multiple sessions of about an hour or less, instead of a massive three-hour binge. Cramming is ineffective because, after a long night of studying, you lose focus and forget most of the information by the following day. The best way to study is to constantly and repeatedly expose yourself to the study material. For increased focus and productivity, taking a break in between study sessions is important.

Another finding after the analysis revealed that the high-achieving students reported having a good concentration level even during vacations. Students might get a lot of benefits from even a little study during vacations. It is easier for them to pick it up after vacations are over. Hence, studying even during your vacations helps keep you connected to your studies.

Our results indicated another trend regarding the duration of breaks taken by the students in between their study times. It is shown that most of the students who had attained high scores (more than 80%) in their previous professional examinations took breaks that were between 30 minutes and an hour long, or even less. A lot of the students with lower academic performance reported taking breaks that were even more than 2 hours long. Short-term deviation from the task might improve concentration levels. The results indicated that the students who had taken breaks of more than 2 hours had just wasted their time, and this had probably resulted in their poor academic performance relative to the high-achieving students. According to a study conducted by Adebayo FA, academic performance seems to increase when time management skills are well-handled.[8]

Another finding of this research was that switching places between studies might benefit you. Repeated studies in the same spot could affect your memory recall adversely. At the time of the examination, the change of location might catch you off guard. A change of surroundings while you study will help in retaining the study material regardless of the environment. Most of the students who had scored highly reported changing places between studies. Our results echo similar results in a study, which stated that studying in different locations can aid in memory recall and learning.[9, 10]

Apart from general study strategies, our research also revealed that day scholars generally score higher than hostellers. This may be because hostellers have to face certain problems like feeling homesick, doing all of their work themselves, and having difficulty with time management, which affect their academic performance. The academics of day scholars and hostellers have been compared in numerous studies by several academic institutes in multiple countries, and the findings have varied. [11] Our results are comparable to a previous study which reported that day scholars to have better study habits as compared to hostellers, and thus, they score higher. [12] In contrast to this, another study was conducted, and the results of the study concluded that hostellers were academically more successful as compared to day scholars. [13] Apart from these, another study indicated that there was no significant difference when it came to the academic achievements of hostellers and day scholars.[11]

This study had some limitations. Even though this study has shown some major trends in study approaches, it is important to note that a study habit for one student may not necessarily work for another. Furthermore, the sample size was insufficient. Other than these, since only survey responses from one institution were used to generate the results, they might not be representative of medical students nationwide.

CONCLUSION

The students achieving higher academic scores studied regularly for about 2-4 hours daily, could concentrate for 1-2 hours at a stretch, preferred switching places during their studies, and took breaks that lasted around 30 minutes. Their study habits were unaffected by vacations. Both medical students and their educators and mentors must consider the results of the study's findings. These findings should ideally be utilized to direct medical students toward productive study skills early in their medical training, enabling them to perform to their greatest potential.

RECOMMENDATIONS

If faculty mentors and instructors have a greater understanding of what study strategies are most beneficial, they will ideally be better able to help students who are having difficulty and even provide students with better suggestions for changing their learning habits to ones that have been proven to be successful.

REFERENCES

1. Abdulghani HM, Al-Drees AA, Khalil MS, Ahmad F, Ponnamperuma GG, Amin Z. What factors determine academic achievement in high achieving undergraduate medical students? A qualitative study. Medical Teacher. 2014 Mar 11;36(sup1): S43–8. https://doi.org/10.3109/0142159X.2014.886011

2. Liles J, Vuk J, Tariq S. Study Habits of Medical Students: An Analysis of which Study Habits Most Contribute to Success in the Preclinical Years. MedEdPublish. 2018;7(1). https://doi.org/10.15694/mep.2018.0000061.1

3. Lerchenfeldt S, Nyland R. Learning Technique Utility and Preferences Among Second-Year Medical Students: A Pilot Study of General and Pre-Exam Study Habits. MedEdPublish. 2016;5(3). https://doi.org/10.15694/mep.2016.000096

4. Grafton-Clarke C, Garner J. Study Skills, Social Life and Confidence in Undergraduate Medical Students. MedEdPublish. 2018;7(3). https://doi.org/10.15694/mep.2018.0000165.1

5. Harvey J, Watt H. Using learning technology to support student study skills. In: Implementing learning technology: Learning Technology Dissemination Initiative. 1st ed. Edinburgh: Heriot-Watt University-1996: 28-34. http://www.icbl.hw.ac.uk/ltdi/implementing-it/support.pdf

6. Smith G. Teaching study skills: a guide for teachers. J Learning Disabilities. 1986 Jun;19(6):381–1. doi:10.1177/002221948601900618

7. Idris A, Saadi TA, Edris B, Sawaf B, Zakaria MhdI, Alkhatib M, et al. Self-reported study habits for enhancing medical students' performance in the National Medical Unified Examination. Avicenna J Med. 2016 Apr;06(02):39–46. https://doi.org/10.4103/2231-0770.179553

8. Florence Aduke A. Time Management and Students Academic Performance in Higher Institutions, Nigeria — A Case Study of Ekiti State. Intern Res Education [Internet]. 2015 Apr 20;3(2):1. https://doi.org/10.5296/ire.v3i2.7126

9. Smith SM, Glenberg A, Bjork RA. Environmental context and human memory. Memory & Cognition. 1978 Jul;6(4):342–53. https://doi.org/10.3758/BF03197465

10. Fowler A, Whitehurst K, Al Omran Y, Rajmohan S, Udeaja Y, Koshy K, et al. How to study effectively. Inter J Surg Oncol. 2017 Jul;2(6):e31. http://doi.org/10.1097/IJ9.0000000000000031

11. Faisal R, Shinwari L, Izzat S. Academic performance of day scholars versus boarders in pharmacology examinations of a medical school in Pakistan. JPMA [Internet]. 2016 Sep 1;66(9):1094–7. Available from: https://pubmed.ncbi.nlm.nih.gov/27654727/

12. Khurshid F, Tanveer A, Qasmi F. Relationship between Study Habits and Academic Achievement among Hostel Living and Day Scholars' University Students. British J Humanities and Social Sci [Internet]. 2012;34(2). Available from: http://www.ajournal.co.uk/HSpdfs/HSvolume3(2)/HSVol.3%20(2)%20Article%204.pdf

13. Bahadar N, Mahnaz W, Jadoon S, Jadoon S. A comparative analysis of the behaviors and performance of day scholar and boarder students at secondary school level. American Jof Educa Res. 2014 July;2(8):600-2.

CONFLICT OF INTEREST: Authors declare no conflict of interest

GRANT SUPPORT AND FINANCIAL DISCLOSURE: NIL

AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under

Mushtaq H: Conceiving and designing the study, col lection, analysis, interpretation of data, Manuscript writing, Approval of Final draft

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

ORIGINAL ARTICLE

METFORMIN MODULATES SERUM CA 19-9 AND ITS RELATED FACTORS MORE EFFECTIVELY THAN GLIBENCLAMIDE IN DIABETIC PATIENTS

Mohammad Waqas[1], Muhammad Idrees[2], Saima Qayyum[2], Muhammad Ihtesham[2], Mohsin Shafi[2], Inayat U Rahman[3]

[1]Khyber College of Dentistry, Peshawar, KP, Pakistan

[2]Department of Pathology, Khyber Medical College, Peshawar, KP, Pakistan

[3]Kabir Medical College, Gandhara University, Peshawar, KP, Pakistan

ABSTRACT

Objective: CA 19-9 is a marker that shows the relapse of tumors. Raised CA 19-9 in diabetes mellitus cases and the effect of hypoglycemic agents on the marker prompted us to compare the effect of metformin and glibenclamide on CA 19-9 levels in patients with diabetes mellitus.

Material & Methods: It is a randomized control trial (RCT). Normal control (group A1) included 40 staff members from KTH/KMC. A total number of 79 patients with type 2 diabetes mellitus were randomized into two groups; group A2 (n=39) who took metformin (500 mg/day) and group A3 (n=40) received glibenclamide (2.5 mg/day). The study was conducted for 6 months and variables including fasting blood glucose, blood lipids, plasma sialic acid, HbA1-c, insulin and C-peptide, CA 19-9, and insulin resistance were measured initially and at week 10.

Results: At the endpoint, there were reductions in FBG and HbA1C levels among metformin and glibenclamide groups compared to baseline ($p<0.003$, $p<0.001$, and $p<0.05$, $p\leq0.05$ respectively). The metformin group also showed a significant reduction in CA 19-9 level from baseline ($p\leq0.05$) and the same was the case for PSA ($p<0.04$) but the effect of glibenclamide on CA 19-9 was negligible and PSA slightly increased (deteriorated) from baseline. Between groups comparison at the endpoint showed a significantly high level of PSA in the glibenclamide group than in the metformin group ($p\leq0.05$). Insulin, HOMA-IR, and C-peptide levels improved in both groups from baseline. The favorable effects of metformin on blood lipids and body weight were more than glibenclamide. Correlation studies revealed a significantly positive correlation ($p\leq0.05$) of CA 19-9 with FBG, HbA1-c, PSA, insulin, and triglyceride levels in the metformin group, and FBG, HbA1-c, PSA, and total cholesterol in glibenclamide group.

Conclusions: From these findings, we suggest greater beneficial effects of metformin on CA 19-9 and other related factors than glibenclamide.

Keywords: CA 19-9, Diabetes mellitus, Glibenclamide, Metformin.

This article may be cited as: Waqas M , Idrees M , Qayyum S, Ihtesham M, Shafi M, Rahman IU. Metformin modulates serum CA 19-9 and its related factors more effectively than glibenclamide in diabetic patients. J Med Sci 2022 July;30(3):212-215

INTRODUCTION

CA 19-9 is a tumor-associated carbohydrate antigen, the serum level of which is elevated among patients with cancer of the ovaries, pancreas, colon and rectum, upper gastrointestinal tract, and liver. It is a tetrasaccharide most commonly attached to O-glycans on the cell surface. Although it is clinically used as a tumor marker of the gastrointestinal tract, its diagnostic sensitivity and specificity are highest for pancreatic cancer. Increased levels are also found in cholecystitis and pulmonary sequestration as well as impaired renal and hepatic functions[1-4].

Literature shows that the levels of CA 19-9 are increased in patients with type 2 diabetes mellitus because of non-tumor factors such as uncontrolled hyperglycemia, lipidemia, and impaired function of pancreatic β-cells. Recently it has been observed that CA 19-9 is correlated with the duration and severity of diabetes as well as the presence of diabetic complications and that the serum concentration is affected by insulin treatment[5,6]. However, the effect of the treatment algorithm on serum CA 19-9 is not properly defined in the literature.

Hence this study was arrangedtoo determine changes in CA 19-9 concentrations and its related factors among type 2 diabetics who are using metformin or glibenclamide.

Correspondence
Dr. Muhammad Idrees
Associate Professor
Department of Pathology, Khyber Medical College, Peshawar, Pakistan
Email: dr.idreeskhan2036@gmail.com
Cell: +92 3349153079
Date Received: 24-08-2022
Date Revised: 06-09-2022
Date Accepted: 22-09-2022

MATERIALS AND METHODS

Of the 203 subjects in Khyber Teaching Hospital (KTH), Peshawar for medical checkups between July 2020 and December 2020, 112 were diagnosed as having type 2 diabetes mellitus without diabetic complications. Seventy-nine met the eligibility criteria and were randomized into the metformin group (n=39) and the glibenclamide group (n=40) (Table1).

Inclusion criteria: Newly diagnosed cases of type 2 Diabetes mellitus with fasting blood glucose of above 126 mg/dl, aged 30-60 years, and having normal renal and liver profiles.

Exclusion criteria: Patients already using glucose-lowering medicine or chemotherapy, those having cancers, diabetic complications (microvascular/macrovascular), gall bladder/thyroidal/GI diseases, genital diseases, pancreatitis, fatty liver, or any other condition causing elevation of CA 19-9.

This randomized controlled parallel-group trial was carried out for 24 weeks. Thirty-three subjects did not meet the inclusion criteria so they were excluded. Seventy-nine participants were randomized into 2 groups; group A2 were given metformin 500 mg/day (26 males/13 females), group A3 received glibenclamide 2.5mg/day (29 males/11 females). Forty healthy subjects (28 males/12 females) from the staff of KTH/KMC, Peshawar served as normal control (group A1).

Fasting (venous) blood specimen was obtained after 12-14 hours of overnight fasting. Different biochemical parameters including fasting blood glucose (FBG), high-density lipoprotein cholesterol (HDL-C), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), and triglyceride (TG) concentrations were determined with OPTIZEN autoanalyzer (2120) using commercially available kits. HbA1c was detected by the Fast ion-exchange resin separation method. Insulin and C-peptide (CP) were determined using the biochemical immune analyzer. CA 19-9 levels were determined by radioimmunoassay. Serum/plasma sialic acid assay (SSA)/(PSA) was performed by using the Warren method. A white blood cell (WBC) count was performed using a hematology analyzer. For insulin resistance, a homeostasis model assessment was used and calculated as Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) = Insulin (μLU/ml) X FBG (mmol/L)/22.5.

Quantitative variables were analyzed using mean and standard deviation, while qualitative variables with frequency and percentages. SPSS 21.0 was used to compile results. P-value < 0.05 was taken as significant. Clinical characteristics of normal controls and diabetic patients were compared using the Independent sample t-test. Mann-Whitney test and Kruskal Wallis test were applied considering the data was not normally distributed among the study groups.

RESULTS

Table 1 and Table 2 show the characteristics of study groups and changes in metabolic variables in diabetic subjects after treatment with metformin or glibenclamide respectively. Table 3 shows the correlation of CA 19-9 with metabolic variables after controlling for age, sex, and BMI. There was positive correlation with HbA1-c ($r=0.171$, $P<0.05$), PSA ($r=0.163$, $P\leq0.05$), insulin ($r=0.151$, $P\leq0.005$) and TG ($r= 0.351$, $\leq P<0.04$) among patients on metformin monotherapy and HbA1-c ($r=0.129$, $P\leq0.05$), PSA (0.155, $P\leq0.05$) and TC ($r=0.389$, $P<0.05$) among patients on glibenclamide monotherapy.

Data are mean ±SD Group A1= Normal control; Group A2= Metformin treated; Group A3= Glibenclamide treated[¤] $p\leq0.05$ vs. Normal control

DISCUSSION

Research shows elevated CA 19-9 concentration in patients of Type II diabetes mellitus than normal control subjects. The exact mechanism remains unclear but several factors are believed to be responsible for this elevation such as hyperglycemia, hyperlipidemia, impaired β-cell function and so forth[5, 7-9]. There is impaired catabolism of CA 19-9 due to the hyper glycation of proteins responsible for its catabolism[6]. A positive association between blood glucose and CA-19-9 and a decline in its concentration with diabetes treatment has been reported previously[10]. Recently, Tu et al[11] have shown that low CA 19-9 is associated with alleviation of insulin resistance in obese patients who are diabetic. Based on these observations, we conducted a study to observe and compare the level of CA 19-9 in newly diagnosed diabetics following metformin and/or glibenclamide monotherapy. The patients on metformin monotherapy manifested a significantly low level of CA 19-9 along with PSA from baseline whereas the patients on glibenclamide monotherapy failed to show significant improvement either in CA19-9 or PSA concentrations, rather the PSA level further deteriorated in glibenclamide group. These findings are well supported by our previous study showing a significantly positive effect of metformin on PSA in type 2 diabetics[12]. We also found a significantly positive correlation of CA 19-9 with HbA1-c, PSA, TC, and HDL-c in diabetic patients and this is in agreement with the previous reports[11]. Based on these findings, we suggest that hyperglycemia and hyperlipidemia induced hyper sialylation is believed to be responsible for increased synthesis of CA 19-9 in diabetics, and a decrease in the process of sialylation by metformin may contribute to a reduction in serum CA 19-9 concentration.

CA 19-9 is released by the pancreas and its level in the body is elevated in many cancerous conditions but has a high sensitivity (70-90%) and specificity (68-91%) for

Table 1: Baseline features of normal control, diabetic patients on metformin and diabetic patients on glibenclamide.

Variables	Group A1	Group A2	Group A3
N	40	39	40
Age	49.50±6.30	51.10±7.80	50±6.10
Sex (M/F)	28/12	26/13	29/11
BMI (Kg/m2)	21.60±0.90	25.70±1.15¤	25.20±0.80¤
Smoking (Cig/day)	35	28	22
Time since diagnosis of diabetes (y)	-	2.1±0.50	2.7±0.10
FBG (mmol/L)	5.09±0.35	9.11±2.60¤	9.24±2.14¤
HbA1-c (%)	6.05±0.70	8.50±0.90¤	8.30±0.95¤
CA 19-9 (U/L)	8.11 (4.77-13.8)	10.58±1.05¤	10.45±1.30¤
SSA/PSA (mmol/L)	2.01±0.10	2.40±0.26¤	2.39±0.19¤
Insulin (μLU/ml)	17.88±4.01	10.95±8.01¤	11.50±16.30¤
HOMA-IR	4.11±1.10	4.97±8.20¤	4.56±11.45¤
CP (ng/ml)	2.59±0.81	1.89±0.95¤	2.01±1.05¤
TC (mmol/L)	4.21±0.78	5.50±1.45¤	4.90±0.95
HDL-c (mmol/L)	1.40±0.25	1.07±0.30	1.22±0.41
LDL-c (mmol/L)	2.44±0.35	2.69±0.68¤	2.54±0.70
TG (mmol/L)	0.78±0.60	2.10±0.45	1.82±0.70

Data are mean ±SD

Group A1= Normal control; Group A2= Metformin treated; Group A3= Glibenclamide treated¤p≤0.05 vs. Normal control

Table 2: Changes in various biochemical/metabolic variables of diabetic patients on metformin and/or glibenclamide monotherapy

Variables	Group A1	Group A2
BMI (Kg/m2)	25.35±0.55 (−0.35)	25.50±0.80 (+0.30)
FBG (mmol/L)	5.90±1.35 (−3.21) *	6.05±1.10 (−3.19) *
HbA1-c (%)	7.60±0.60 (−0.90) *	7.45±0.80 (−0.85) *
CA 19-9 (U/L)	9.11±1.40 (−1.46) *	9.77±1.85 (−0.68)
SSA/PSA (mmol/L)	2.15±0.13 (−0.25) *	2.42±0.21 (+0.03) †
Insulin (μLU/ml)	13.20±6.50 (+2.25)	13±7.90(+1.50)
HOMA-IR	4.60±8.50 (−0.37)	4.30±10.70 (−0.26)
CP (ng/ml)	2.15±0.66 (+0.26)	2.12±0.80 (+0.11)
TC (mmol/L)	4.55±0.74 (−0.95) *	4.91±0.70 (+0.01)
HDL-c (mmol/L)	1.24±0.45 (+0.17)	1.10±0.60 (−0.12)
LDL-c (mmol/L)	2.50±0.30 (−0.19)	2.61±0.55 (+0.07)
TG (mmol/L)	1.35±0.50 (−0.65) *	1.95±0.90 (+0.13) †

Data are mean ±SD Group A2= Metformin treated; Group A3= Glibenclamide treated

() Change from baseline

*P≤0.05 Baseline vs. Post-treatment

†P≤0.05 Group A2 vs. Group A3

Table 3: Partial correlation of CA 19-9 with metabolic variables in diabetic subjects on metformin or glibenclamide monotherapy after controlling for age, sex, and BMI

Variables	Group A2		Group A3	
	r	p	r	p
FBG (mmol/L)	0.151	<0.002	0.130	<0.001
HbA1-c (%)	0.171	<0.05	0.129	≤0.05
SSA (mmol/L)	0.163	≤0.05	0.155	≤0.05
Insulin (μLU/ml)	0.151	≤0.05	0.146	<0.06
HOMA-IR	0.209	<0.16	0.195	0.13
CP (ng/ml)	0.110	<0.21	0.108	<0.14
TC (mmol/L)	0.271	<0.11	0.389	<0.05
HDL-c (mmol/L)	-0.264	0.14	0.100	0.31
LDL-c (mmol/L)	0.31	<0.06	0.409	<0.23
TG (mmol/L)	0.351	≤0.05	0.293	<0.09

pancreatic cancer[3,13,14]. Sialic acid is an acetylated form of neuraminic acid. Its level in the blood rises in cancer and diabetic patients and is a reputable tumor marker as well as a cardiovascular risk factor[15, 16]. Studies indicate that sialic acid regulates vessel wall permeability. Raised levels of sialic acid are present in the vascular endothelium and type 2 diabetes-associated extensive microvascular damage may be responsible for its shedding into the circulation. The result is an increase in vascular permeability and high SSA concentrations[17, 18]. Our findings are further strengthened by the fact that the use of metformin is as-

sociated with longevity in diabetic patients who have pancreatic carcinoma. [19].

CONCLUSION

These findings suggest that metformin modulates CA 19-9 and its related factors more effectively than glibenclamide suggesting the former to be a preferred choice in the prevention of diabetic complications than the latter. Further multicentre studies are required on a large scale to validate the data regarding the effects of metformin in modulating CA19-9 and eventually preventing diabetic complications.

REFERENCES

1. Locker GY, Hamilton S, Harris J, Jessup JM, Kemeny N, Macdonald JS et al. ASCO 2006 update of recommendations for the tumor markers in gastrointestinal cancer. J Clin Oncol, 2006; 24: 5313-27.
2. Turgutalp K, Ozhan O, Helvaci I, Ata A, Arican A, Boztepe B et al. Serum levels of cancer biomarkers in diabetic and non-diabetic proteinuric patients: a preliminary study. Clin Chem Lab Med, 2013; 51: 889-95.
3. Goonetilleke KS, Siriwardena AK. Systematic review of carbohydrate antigen (CA19-9) as a biochemical marker in the diagnosis of pancreatic cancer. Eur J Surg Oncol, 2007; 33: 266-70.
4. Murohisa T, Sugaya H, Tetsuka I, Suzuki T, Harada T. A case of common bile duct stone with cholangitis presenting an extraordinarily high serum CA19-9 value. Intern Med, 1992; 31: 516-20.
5. Gul K, Nas S, Ozdemir D, Gumus M, Ersoy R, Cakir B. CA19-9 level in patients with type 2 diabetes mellitus and its relation to metabolic control and microvascular complications. Am J Med Sci, 2011; 341: 28-32.
6. Murai J, Soga S, Saito H, Otsuki M, Kitada T, Saisho Y et al. Study on the mechanism causing elevation of serum CA 19-9 levels in diabetic patients. J Endocrine, 2013; 60 (7): 885-91.
7. Uygur BO, Dabak R, Orbay E, Dolapçıoğlu C, Sargın M, Kılıçoğlu G et al. Type 2 diabetes mellitus and CA19-9 levels. World J Gastroenterol, 2007; 13: 5357-9.
8. Huang CK, Xu Y, Bi Y, XU M, LU J, WANG T et al. Relationship between CA19-9 levels and glucose regulation in a middle aged and elderly Chinese population. J Diabetes, 2012; 4: 147-52.
9. Yu H, Li R, Zhang L, Chen H, Bao Y, Jia W. Serum CA19-9 level associated with metabolic control and pancreatic beta cell function in diabetic patients. Exp Diabetes Res, 2012; 745189.
10. Benhamou PY, Vuillez JP, Halimi S P Y, Meffre G, Bachelot I. Influence of metabolic disturbances of diabetes mellitus on serum CA19-9 tumor marker. Diabetes Metab, 1991; 17: 39-43.
11. Tu Y, Yu H, Zhang P, Di J, Han X, Wu S et al. Decreased serum CA19-9 is associated with improvement of insulin resistance and metabolic control in patients with obesity and type 2 diabetes after Roux-en-Y gastric bypass. J Diabetes Invest, 2014; DOI: 10.1111/jdi.12200.
12. Rahman IU, Malik SA, Bashir M, Khan RU, Idrees M. Serum sialic acid changes in type2 diabetic patients on metformin or rosiglitazone treatment. J Clin Pharm Ther, 2010; 35: 685–90.
13. Ventrucci M, Pozzato P, Cipolla A, Uomo G. Persistent elevation of serum CA 19-9 with no evidence of malignant disease. Dig Liver Dis, 2009; 41: 357–63.
14. Goonetilleke KS, Siriwardena AK. Systematic review of carbohydrate antigen CA 19-9 as a biochemical marker in the diagnosis of pancreatic cancer. Eur J Surg Oncol, 2007; 33: 266–70.
15. Gopaul KP, Crook MA. Sialic acid: a novel marker of cardiovascular disease? Clin Biochem, 2006; 39(7):667-81.
16. Painbeni T, Gamelin E, Cailleux A, Le Bouil A, Boisdron-Celle M, Daver A et al. Plasma sialic acid as a marker of the effect of the treatment on metastatic colorectal cancer. Eur J Cancer, 1997; 33(13): 2216-20.
17. Yarema K. The sialic acid pathway in human cells. Baltimore, John Hopkins University; 2006.
18. Lindberg G, Eklund GA, Gullberg B, Rastam L. Serum sialic acid concentration and cardiovascular mortality. Br Med J, 1991; 302:143-6.
19. Sadeghi N, Abbruzzese JL, Yeung SC, Hassan M, Li D. Metformin use is associated with better survival of diabetic patients with pancreatic cancer. Clin Cancer Res, 2012; 18(10): 2905-12.

CONFLICT OF INTEREST: Authors declare no conflict of interest

GRANT SUPPORT AND FINANCIAL DISCLOSURE: NIL

AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under

Waqas M:	Conception, literature search and overall supervision
Idrees M:	Writing up
Qayyum S:	Data collection
Ihtesham M:	Statistical analysis
Shafi M:	Bibliography
Rahman IU:	Data collection

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

ORIGINAL ARTICLE

EFFECT OF H. PYLORI PROTEINS JHP 0290 (FL) AND JHP 0290 ON HOST CELL BEHAVIOR

Muhammad Idrees[1], Mohammad Waqas[2], Inayat U Rahman[3], Muhammad Ihtesham[1], Muhammad Tariq Masood Khan[4], Rashid Azeem[5]

[1]Department of Pathology, Khyber Medical College, Peshawar - Pakistan

[2]Khyber College of Dentistry, Peshawar, KP - Pakistan

[3]Kabir Medical College, Gandhara University, Peshawar, KP - Pakistan

[4]Department of Pathology, Pak International Medical College, Peshawar - Pakistan

[5]Department of Pathology, Peshawar Institute of Cardiology, Peshawar - Pakistan

ABSTRACT

Objective: This study was designed to investigate the effect of H. Pylori proteins JHP 0290 (FL) and JHP 0290 on host cell response.

Materials and Methods: This study was conducted at Khyber Teaching Hospital (KTH), Peshawar from April 2021 to September 2021. H. Pylori genomic DNA (J99 and 26695), pET expression system plasmid (PET21a, 22b & 28b+), kanamycin 50μg/ml and ampicillin 100μg/ml, LB agar plates and LB media, Talon@IMAC resin column were used for studying H. pylori proteins. Genes coding for these proteins were successively cloned into PET21a, PET22b, and PET28b+ expression vectors but no expression was seen with different concentrations of IPTG in BL21(DE3) culture, and expression was prolonged for 4hrs.

Results: Only JHP0290 (FL) & JHP0290 (-17a.a) were successively cloned in PET28b+ and expression was induced by using 100μM IPTG in E.coli strain (BL21DE3). Restriction analysis showed the size of JHP0290 (FL & -17a.a) at approximately 550bp and protein size was analyzed on SDS-page which was 20Kda approximately. JHP0290FL protein was found in pellets while JHP0290 (-17a.a) protein was found in pellets & supernatant before being applied to Talon cell through resin column to get purified protein. The study showed a clear band of JHP0290 (FL) on SDS-page with imidazole eluted fraction pooled, while a faint band with a distinct band of JHP0290 (-17a.a) was also seen on SDS-page.

Conclusion: These changes are indicative of altered host cell response induced by H.pylori protein JHP0290 suggesting its possible involvement in the development and severity of the disease.

Keywords: H.pylori proteins, virulence factor, host cell response, genomic DNA, pathogenicity.

This article may be cited as: Idrees M, Waqas M, Rahman IU, Ihtesham M, Khan MTM, Azeem R. Effect of H. Pylori proteins JHP 0290 (FL) and JHP 0290 on host cell behavior. J Med Sci 2022 July;30(3):216-221

INTRODUCTION

Various gastric diseases such as chronic gastritis, peptic ulcer, gastric cancer, and mucosa-associated lymphoid tissue lymphoma are caused by H. pylori.[1-3] H. pylori is present in about 70% of the world's population[4]. Because of its heterogeneous nature, H. pylori is perfectly adapted for survival in the gastric environment, and for the same reason, it is not so easy to detect the major bacterial factors that are directly associated with etiopathogenesis[5,6]. Virulence factors such as genes within the cag (cytotoxin-associated antigen) pathogenicity island encoding for CagA protein, polymorphic variation in the VacA vacuolating exotoxin, and the blood group antigen binding adhesions (BabA, SabA) are all possible bacterial factors[7,8]. In addition, duodenal ulcer-promoting gene (dupA), bacterial factors such as peptidoglycan, lipopolysaccharide (LPS), g-glutamyl trans-peptidase (GGT), and protease HtrA are all possible causes of pathogenicity[9,10,11]. The presence of these virulence factors is variable among H pylori found in different geographic areas and ethnic groups thus explaining the differences in disease prevalence among individuals e.g., Inhabitants of East Asia have the highest rate of gastric cancer in the world where almost all H. pylori isolates are cagA genopositive, vacA s1/i1/m1 and BabA expressing[12]. In order to understand the pathogenic mechanism of H.pylori, it is very important to identify and

Correspondence
Dr. Mohammad Waqas
Assistant professor
Department of Pathology, Khyber College of Dentistry,
Peshawar, KP - Pakistan
Phone: +92-333-9231747
Email: dr.waqasmarwat1984@gmail.com
Date Received: 21-08-2022
Date Revised: 11-09-2022
Date Accepted: 26-09-2022

determine the functions of all proteins present in their cell. The exact and complete identification of proteins secreted by H. pylori is difficult because of its high lysis frequency that shows the outcome of the nonspecific release of all cytoplasmic proteins[13]. One protein which has been reported in the external medium by different researchers is HP1286. The prime sequence shows that HP1286 tends to belong to Y-Cell like a family of protein [14]. Structurally the Y-Cell like family is a subgroup of the lipocalin superfamily. Lipocalin has a prototype which is a retinol-binding protein (RBP) present in the plasma of higher animals [15].

Gastric inflammation and epithelial damage contribute to the secretion of proteins by H. pylori. Urease subunit beta UreB is a known cytoplasmic protein that has 0.25 ratios in the supernatant as that of the pallet and later on, it was considered a lysis index.

The ratio greater than UreB was used to differentiate specific proteins selectively released into the medium. About sixteen different proteins were found in the supernatant. These proteins may be implicated by H. Pylori-induced effects on gastric epithelium [16]. The aim of the study was to investigate how H. pylori proteins JHP 0290 (FL) and JHP 0290 affect the host cell response.

MATERIALS AND METHODS

This study was conducted at Khyber Teaching Hospital (KTH), Peshawar from April 2021 to September 2021. Two strains of H. Pylori genomic DNA (J99 and 26695), pET expression system plasmid (PET21a, 22b & 28b+), kanamycin 50μg/ml, and ampicillin 100μg/ml, Lysogeny Broth (LB) agar plates and LB media, Talon@ IMAC resin column were used.

AMPLIFICATION OF GENES USING PCR

H. pylori genomic DNA from the strain of J99 and the gene coding for JHP0290 (Full length & 18-184a.a) was amplified by PCR using high fidelity DNA polymerase from Finnzymes®. The forward and reverse primers contained NdeI and XhoI restriction enzyme recognition sequences sites. Isolation of circular and recombinant plasmid from DH5α

A single colony from a selective plate of plasmid in DH5α was taken and inoculated into 10ml LB media containing antibiotics (50μg/ml kanamycin or 100μg/ml ampicillin depending upon selection marker) followed by overnight incubation at 37°C with a shaking speed of 150 rpm. The vector was isolated from overnight culture by using the Omega-biotek plasmid miniprep Kit-I following the manufacturer's instructions [17].

Restrictive Digestion of Genes with XhoI and NdeI The restriction enzymes FastDigest XhoI and NdeI were used to digest the insert. The digestion was performed according to the protocol of Fermentas®. The digestion mix was then incubated at 37°C for 2 hours and analyzed on 1% agarose gel with undigested & 1Kb marker. Restrictive Digestion of Expression vector (pET system) with XhoI & NdeI

The expression vector (pET system) was also digested with the same restriction enzymes as with the insert to facilitate ligation. Purified 1.5μg of plasmid DNA was used to digest with XhoI & NdeI. After incubation for 1 hr, the total volume of the digested vector was loaded on the 1% agarose gel. The PCR products and digested plasmids from the gels were then purified by Gelifesciences PCR purification kit. Finally, the concentration of DNA (PCR products & pET plasmids) was quantitatively measured at 260 nm & 280 nm with nuclease-free water as a reference. Purification of PCR Products and plasmid (Quantification of DNA)

The purified and digested PCR products were cloned into pET expression vectors. The molar ratio (5:1) was used to ligate insert into the vector. Fermentas protocol for ligation was used to ligate the gene into the expression vector. The ligation mix was then incubated at 16^{0}C overnight and one without ligase enzyme as a negative control to test self-ligation. After overnight incubation, a ligation mix was used to transform DH5α competent cells.

Preparation of E.coli [DH5α + BL21 (DE3)] competent cells E.coli strains [DH5α + BL21 (DE3)] were supplied by Novagen and followed the method proposed earlier [18].

Transformation in DH5α competent cells The ligation mix 10μl was inoculated into 100μl DH5α competent cells and kept on ice for 30 minutes, followed by a heat shock at 42^{0}C for 1 min. The transformation was carried out as described earlier [19].

PCR analysis of clones 20 blocks were drawn on an LB agar plate containing kanamycin (50μg/ml) and a single colony was taken from a ligation mix plate and streaked on the blocks followed by inoculating the same loop containing the inoculum into a sterile Eppendorf tube having 20μl nuclease-free water. After that, Eppendorf tubes were incubated at 95^{0}C for 10 minutes, followed by centrifugation at 13000 rpm for 2 minutes. 2μl from supernatant from each Eppendorf tube was taken and used as template DNA in PCR reaction mix for verification of successful ligation and clone [20]. 12 colonies were taken from the ligation mix and one from positive control (circular Jhp0290 FL in PET28b+). After PCR cycle completion, PCR samples were loaded with 6x loading dye on 1% agarose gel for the verification of clones.

Recombinant plasmid isolation, gene amplification, and restriction analysis of clones 2,4,6,8 (Jhp0290-17a.a) no. clones were selected for plasmid isolation and amplification of gene of insert (Jhp0290-17a.a). PET28b+ (Jhp020 (-17a.a) clones (2, 4, 6 & 8) were inoculated into 10 ml LB media containing 50μg/ml Kanamycin (10μl) followed by incubation inside at 37°C incubator with shaking for overnight. Using Omega-biotek plasmid miniprep Kit-I, the plasmid was isolated following manufactures specification to analyze the band of interest [21].Transformation of Recombinant Plasmid in BL21 (DE3) competent cells

2, 4 (Jhp0290-17a.a in PET28b+) clones were selected for transforming in BL21 (DE3) competent cells and induced expression upon the addition of IPTG. The purified recombinant circular plasmid 1μl (80ng of DNA) was inoculated into 100μl BL21(DE3) competent cells and kept on ice for 30mins followed by a heat shock at 42^{0}C for 1 min. Then 400μl of pre-warmed LB media was added to the transformation mix and kept the mix at 37^{o}C with a shaking speed of 150 rpm/ hour. After 1 hour, 250μl reaction mix was placed on LB agar plates containing kanamycin (50μg/ml), and glycerol stock of JHP0290 FL in PET28b+ was also streaked on LB agar plate containing Kanamycin followed by incubation for overnight. After overnight incubation, colonies appeared 148 on 2 no. clone plates and 158 on 4.

Small scale (rapid) and large scale expression of Jhp0290 (-17a.a) and Jhp0290 (FL) These were carried out as described earlier for analysis of protein induction[21].

Purification of recombinant protein Jhp0290 (-17a.a) and Jhp0290 (FL) Jhp0290 (-17a.a) & FL proteins were purified by using the Clontech Talon manual and followed the instruction of usage [22]

Purification of protein Jhp0290 (-17a.a) and Jhp0290 (FL) TALON cell through resin TALON is an immobilized metal affinity chromatography (IMAC) resin charged with cobalt, which binds to his-tagged proteins with higher specificity than nickel-charged resins. As a result, TALON resin delivers his-tagged proteins of the highest purity [23]. Data were analyzed using Graph Pad Prism version 9.2.0 and Graph Pad InStat version 3.10.

RESULTS

After completion of PCR cycles, the samples were loaded on 1% agarose gel with a 1kb marker. PCR products were successfully amplified by Phusion high-fidelity DNA polymerase. PCR product was around 550bp in size which was compared to 1Kb 500bp marker band size as a reference. The amplified PCR products were further purified from the gel by Omega bio-tek and digested with XhoI & NdeI restriction enzymes at 37^{o}C. The digested vector was loaded on 1% agarose gel and digestion was carried out for further analysis. For the ligation of the construct into the PET expression vector, 80-100ng of plasmid and 35-45ng of PCR product were used. The construct was successively ligated into PET28b+. Colonies appeared on positive control (full lawn); ligation mix and no colonies were obtained on self-ligated mix plates.

PCR analysis of Clones12 colonies were taken from a ligation mix plate & one with positive control and used for PCR analysis of clones. PCR analysis was successful and bands of insert (Jhp0290-17a.a & FL) were seen on the gel. The size of colony bands was 550bp compared to the band of 500bp on the 1Kb ladder (Figure 1).

Plasmid amplification and purification The plasmid-containing insert was amplified and purified using the Omega-biotek plasmid miniprep Kit-I spin protocol. Quantification of the plasmid DNA was yielded in Table 1.

Amplification of insert from recombinant plasmid 2, 4, 6 & 8 clones (Jhp0290-17a.a in PET28b+ & positive FL) were selected for PCR to verify the correct size of gene of interest and PCR reaction mix protocol was the same as that for Colony PCR. PCR reaction yielded 550bp fragment on 1% agarose gel. On the 6th lane positive control was loaded and similar band can be seen with size range of 550bp (Figure 2).

Restriction analysis of Clones Recombinant plasmid was digested with two restriction enzymes XhoI & NdeI and loaded on 1% agarose gel that yielded 550bp and 5.4kb fragments in first four lanes after 1Kb ladder marker. On 6th lane a positive control (Jhp0290FL in PET28b+) also yielded 550bp fragment and no fragment occurred in negative control (Figure 3).

Small scale expression of Jhp0290-17a.a & Jhp0290 FL and SDS-page Two clones (Jhp0290-17a.a in PET28b+) were induced under the control of 100μM & 500μM IPTG at 2.5hrs incubation at 37^{o}C and one without IPTG with 0 hour & 2.5 hrs incubation times. The insert (Jhp0290-17a.a) was induced at 100μM & 500μM IPTG concentration and compared with uninduced at 0 & 2.5hrs time incubation. The size of the expression of gene is 20Kda approx. There is no expression of gene in un-induced at 37^{o}C at 0 hr & 2.5hrs (Figure 4).

Figure 5 shows the 2, 4 clones (Jhp0290-17a.a in PET28b+) induced by IPTG with 100μM & 500μM concentration and one clone (Jhp0290 FL in PET28b+) with 100μM IPTG concentration. The gene of interest was expressed at 100μM & 500μM but no expression seen in uninduced sample at 0hr & 2.5hrs at 37^{o}C. Large scale expression of Jhp0290-17a.a & Jhp0290 FL and SDS-page

In large scale expression of Jhp0290-17a.a & FL, overnight culture was inoculated into 500ml LB media containing 50μg/ml kanamycin and culture was induced with 100μM IPTG at 37^{o}C with shaking for 2.5hrs. No expression was seen in uninduced sample (Figure 6). Purification of recombinant protein Jhp0290 (-17a.a)

A clarified sample was prepared from a pellet containing Jhp0290 (-17a.a) protein and then loaded on 12% polyacrylamide gel. On the 1st lane marker, uninduced, induced samples and pellet and the supernatant was loaded to know the solubility of the protein. Pellet and supernatant showed a clear band of Jhp0290. Protein from the supernatant was further purified by Talon Resin column. The induced sample showed a clear band and 2nd fraction of elution also showed cleared band. No band showed in uninduced, flow thru, elution 1. In elution 3rd fraction, a similar size band was also seen but not distinct (Figure 7 & 8).

DISCUSSION

In this study, H. Pylori strains J99 and 26696 were used and genes coding for Jhp0290 (-17a.a & FL) were amplified by using Phusion high fidelity DNA polymerase. High-Fidelity DNA Polymerases are important for applications in which the DNA sequence needs to be corrected after amplification [24,25]

Our results showed a clear band on 1% agarose gel after PCR reaction. Genes coding for HP1206 (FL & signal peptide) and HP0305 were successively digested, ligated, and cloned into pET22b & pET21a. Colonies were observed after transformation in E.coli strain (DH5α & BL21(DE3) competent cells, but there was no expression seen at 100μM, 250μM, 500μM, and 1mM concentration of IPTG at 30°C & 37°C with shaking for 3-4hrs. T

he experiment was repeated and the gene coding for J0290-17a.a & FL was amplified by using Phusion DNA polymerase. PCR products were used to clone

Table 3: Amplification and purification of plasmid

Clone	280/260	230/260	DNA
2	**1.87**	1.90	85.17ng/μl
4	1.86	1.83	81.88
6	1.89	1.84	78.77
8	1.86	1.84	75.47

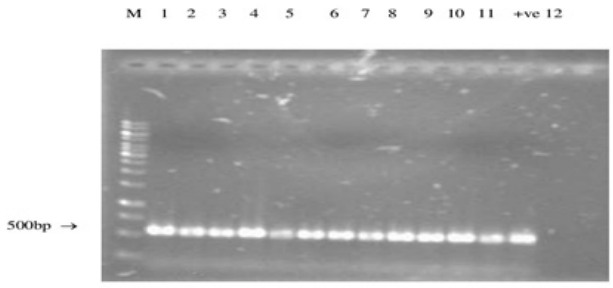

Fig 1: PCR analysis of clones, M= 1Kb Ladder, 1-11 Ladder, 1-11 & 12 represent Jhp0290 (-17a.a) and +ve control = Jhp0290 FL sample were loaded on 1% agarose gel for the verfication of colonies

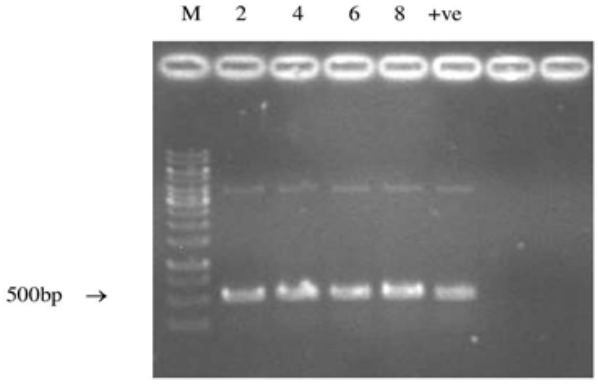

Fig 2- Amplification of insert in recombinant plasmid using PCR, M (1kb Ladder), 2,4 6 & 8 (Jhp0290-17a.a) and +ve control (Jhp0290FL) samples were loaded on 1% agarose gel for the analysis of amplified insert.

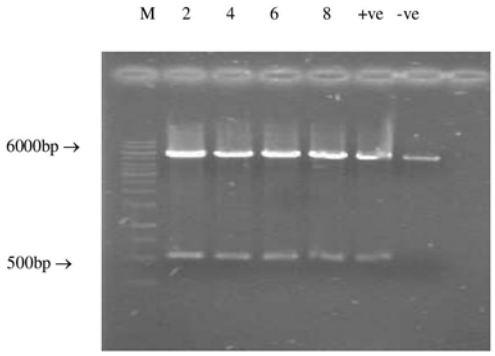

Fig 3- Restriction analysis of clones with XhoI and NdeI restriction enzymes; M=1kb ladder, 2,4,6,8 (Jhp0290-17a.a in PET28b+) +ve (Jhp0290FL in PET28b+) and -ve (PET28b+) samples were loaded on 1% agarose gel

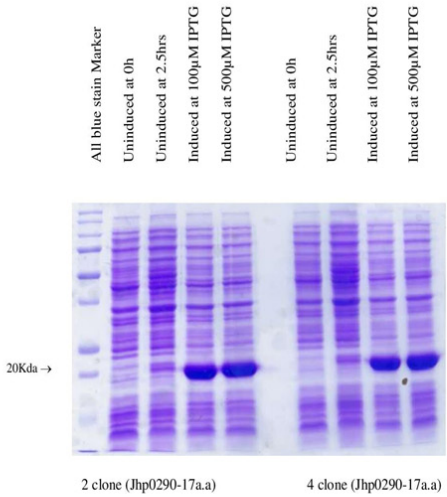

Fig. 4. On the 1st lane, all stain blue marker, 2, 4 clone's uninduced at Oh, uninduced at 2.51rs, induced at 100pM & 500pM IPTG was loaded on 12% separating gel for SDS-page analysis.

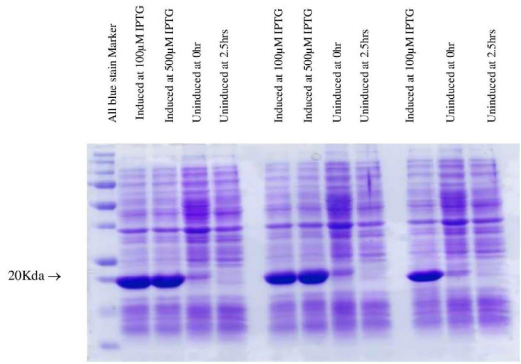

Fig. 5. All blue prestained marker (Biorad) was loaded on l't lane. On successive lanes samples induced with 100pM & 500pM IPTG concentration after 2.5hrs of incubation at 37°C with shaking, loaded on 1% agarose gel. Uninduced samples at Oh & 2.5hrs incubation were also loaded.

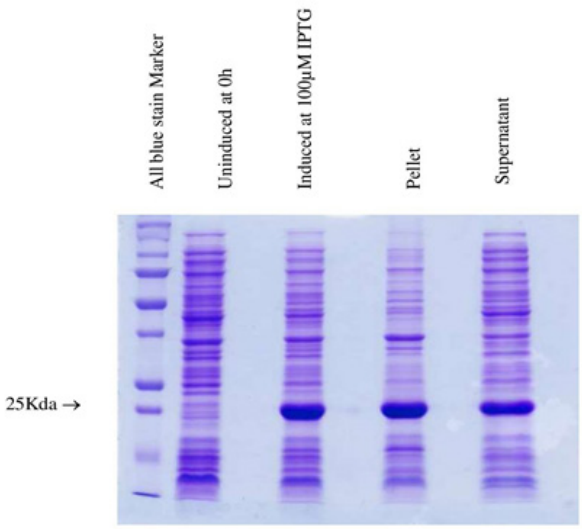

Fig 6- Large scale expression of Jhp0290-17a.a Fl analysis on SDS-Page

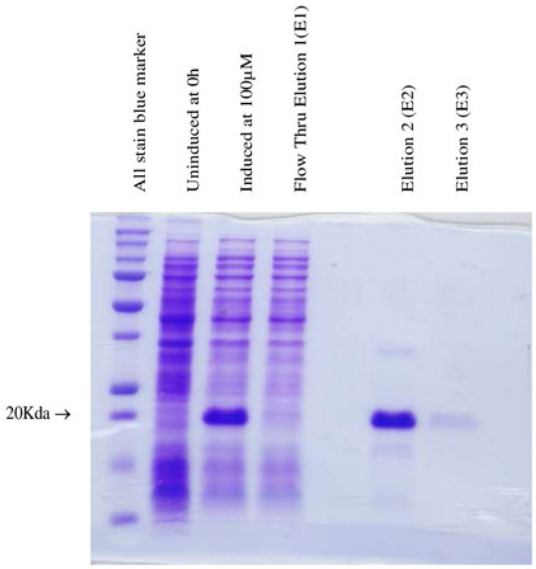

Fig 7- Analysis of protein purification on SDS-Pege

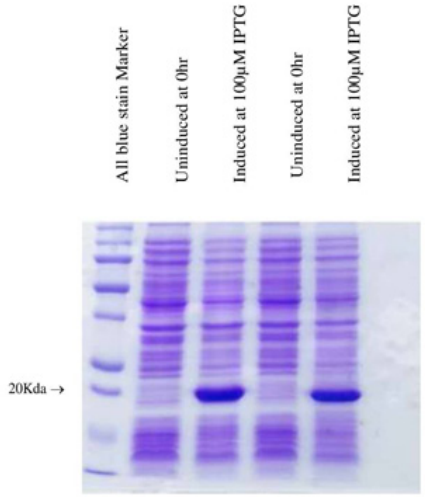

Fig 8- Purification of protein through Talon resin column and analysis on SDS-Page

into pET28b+ vector and transformed into DH5α & BL21 (DE3). Colonies appeared on the LB agar plates with kanamycin (50μg/ml) as a resistance marker strengthening the previous findings by Rourke et al and further experiments were performed to induce the expression of a gene with 100μM to 1mM IPTG concentration[26]. Sometimes, no expression of genes was seen on SDS polyacrylamide gels, and then sequencing of the cloned gene was done by a clinical company.

The results of sequencing showed that there was an error in the gene which ultimately did not induce the expression. The experiments were repeated. Purified plasmid (with 260/280 & 260/230) and the gene coding for Jhp0290 ((-17a.a) were digested with XhoI & NdeI restriction enzymes at 37°C for one hour for plasmid and 2 hours for PCR products that produced blunt ends as carried out earlier by Hamidi et al [27]. Plasmid and PCR product was purified and ligation was performed at 16°C overnight by using T4 DNA ligase. The ligation method was performed at 22°C but showed no colonies on LB agar plate with kanamycin resistance marker because of linear DNA death and showed no resistance to antibiotics. Ligation at 16°C worked well and proceeds further. Colony PCR was performed to verify the selection of good clones and restriction digestion of selected clones to verify the size of the insert. Colony PCR and restriction digestion yielded the same 550bp fragment and the remaining 5.4Kb fragment.

The induction of gene (Jhp0290 -17a.a) expression was noted at 100μM & 500μM IPTG concentration on a small scale. Large-scale expression of the gene was performed at 100μM IPTG concentration and the culture was centrifuged to obtain pellets[28]. Pellets containing Jhp0290 (-17a.a & FL) were dissolved in 1x equilibration buffer and sonicated at 4°C with 30% efficiency for 30 seconds with a one-minute pause for each sonication. Samples were centrifuged to get clarified samples to observe the availability of pellets or supernatant. Jhp0290 (-17a.a) was available in pellets and supernatant but Jhp0290 (FL) was in pellets only. Jhp0290 (-17a.a) was purified as a native protein by using Talon cell thru resin that produced a clear band of highly purified Jhp0290 (-17a.a) protein. The size of protein on SDS polyacrylamide was 22.2Kda and a small faint band was also seen above the clear band.

CONCLUSION

These findings suggest that the expression and release of H.pylori proteins JHP 0290 (FL) and JHP 0290 were different among the strains that alter the host cell response to a variable extent. The development and severity of the disease may be attributed to the level of expression of H.pylori secreted proteins as well as the degree of altered host cell response.

The present research work is an expansion of the existing studies and a significant contribution toward explaining how H. pylori proteins affect the host cell response and provides a framework for future research.

REFERENCES

1. Ishaq S, Lois N. Helicobacter pylori and gastric cancer: a state of the art review. Gastroenterol Hepatol Bed Bench.2015, 8: S6-S14.

2. Diaz P, Valderrama MV, Bravo J, Quest AFG. Helicobacter pylori and Gastric Cancer: Adaptive Cellular Mechanisms Involved in Disease Progression. Front Microbiol. 2018, 9: 5.

3. Tsay WF, Hsu PI. H. pylori infection and extra-gastroduodenal diseases. J Biomed Sci. 2018.25: 65.

4. Ansari S, Yamaoka Y. H Pylori virulence factors exploiting gastric colonization and its pathogenicity. Toxins. 2019. 11(11): 677.

5. Kao CY, Wu JJ. H. Pylori infection: An overview of bacterial virulence factors and pathogenesis. Biomedical J. 2016. 39: 14-23.

6. Wen S, Moss SF. H. pylori virulence factors in gastric carcinogenesis. Cancer Lett. 2009. 282: 1–8.

7. Lu H, Hsu P I, Graham DY, Yamaoka Y. Duodenal ulcer promoting gene of H. pylori. Gastroenterology. 2005. 128: 833–48.

8. Yamaoka Y. Mechanisms of disease: H. pylori virulence factors. Nat. Rev. Gastroenterol Hepatol. 2010.7: 629–41.

9. Backert S, Clyne M. Pathogenesis of H. pylori infection. Helicobacter. 2011.1: 19–25.

10. Cremades N, Campoy AV, Martinez-Julvez M, Neira J L, Perez-Dorado I, Hermoso J.Discovery of specific flavodoxin inhibitors as potential therapeutic agents against Helicobacter pylori infection. ACS Chem Bio. 2009.4: 928–38.

11. Han KD, Matsuura A, Ahn HC, Kwon AR, Min YH, Park HJ. Functional identification of toxin-antitoxin molecules from H. pylori 26695 and structural elucidation of the molecular interactions. J Biol Chem. 2011. 286: 4842–53.

12. Chang WL, Yeh YC, Sheu BS. The impacts of H. pylori virulence factors on the development of gastroduodenal diseases. J Biomed Sci. 2018.25(1): 68.

13. Nayoung K, David WI, Jai Moo S, David R, Scott I. Proteins released by H. Pylori In vitro. J Bacteriol. 2002. 184: 6155–62.

14. Chong M, Leung R, Wong C, Yuen A. The Effect of ampicillin versus tetracycline on the Plasmid Copy Numbers of pBR322. JEMI. 2002.3: 87-95.

15. Niraj HT, Leemor JT. Strategies for protein co-expression in E. coli. Cold Spring Harbor Laboratory Press. 2006. 3: 1.

16. Sambrook J, Russell DW. Molecular Cloning, A Laboratory Manual. Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY. 3ed. 2001.

17. Sambrook J, Fritsch EF, Maniatis T. Molecular Cloning: A Laboratory Manual. Cold Spring Laboratory, Cold Spring Harbor, NY. 2ed. 1989

18. Tolia NH, Joshua-Tor L. Strategies for protein co-expression in E coli. Nature Methods. 2006. 3: 55-64.

19. Greener A, Callahan M, Jerpseth B. An efficient random mutagenesis technique using an E. coli mutator strain. Mol Biotech. 1997, 7: 189–97.

20. Lodish H, Berk A, Zipursky SL. Polymerase Chain Reaction: An Alternative to Cloning. Molecular Cell Biology, W H Freeman, 4th ed. 2000

21. Sugar FJ, Jenney FE, PoolelI FL, Brereton PS, Izumi M, Shah C, et al. Comparison of small- and large-scale expression of selected Pyrococcus furiosus genes as an aid to high-throughput protein production. J Struct and Funct. Genomics2005. 6: 149- 58.

22. Albert's B, Bray D, Lewis K, Raff M. In: Molecular Biology of the Cell. Garland Publishing, N Y. 1994. 3: 195–222.

23. Bush G L, Tassin A M, Friden H, Meyer DI. Secretion in yeast: purification and in vitro translocation of chemical amounts of pre-pro-alpha factor. J Biol Chem. 1991. 266: 13811-4.

24. Chester N, Marshak D R. Analytical Biochemistry. 1993, 209: 284-90.

25. Frey B, Suppman B. Bio Chemica.199.2: 34-5.

26. Rourke EJ, Pinto AV, Petroni EA, Marcelo ET, Ielpi L. Evidence for the active role of a novel nuclease from H. pylori in the horizontal transfer of genetic information. J Bacteriol. 2004, 9: 2586–93.

27. Hamidi B, Ebrahimi F, Hajizadeh A, Alikhani H K. Fusion and cloning of the binding domains of botulinum neurotoxin type A and B in E. coli DH5α. Euro J Experi Biology. 2012, 2: 1154-60.

28. Ausubel FM, Brett R., Kingston RE, Moore DD, Seidman J G, Smith J A, et al. Current Protocols in Molecular Biology, Johns Wiley & Sons, NY. 1995, 29.

CONFLICT OF INTEREST: Authors declare no conflict of interest

GRANT SUPPORT AND FINANCIAL DISCLOSURE: NIL

AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under

Idrees M:	Project design, Critical review, analysis of data
Waqas M:	Conception, literature search and overall supervision
Rahman IU:	Writing up
Ihtesham M:	Statistical analysis
Khan MTM:	Bibliography
Azeem R:	Data collection

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

ORIGINAL ARTICLE

GENDER BIAS DURING ASSESSMENTS IN UNDERGRADUATE MEDICAL EDUCATION: A QUALITATIVE STUDY

Bibi Aliya[1], Brekhna Jamil[2], Farooq Ahmed[3], Lubna Kashif[3]

[1]Department of community medicine, Rehman Medical College, Peshawar - Pakistan

[2]Department of Institute of Health Professions Education and Research, Khyber Medical University, Peshawar - Pakistan

[3]Department of Medical Education, Khyber Medical College, Peshawar - Pakistan

ABSTRACT

Objective: To explore the perceptions of students and faculty about gender bias during assessments in undergraduate medical education.

Material and Methods: The study was conducted at a Public and Private Medical College in Peshawar, Khyber Pakhtunkhwa Pakistan, from June 2020 to October 2020. It was a qualitative study with a phenomenological approach in which, 4 focal group interviews with undergraduate medical students and 10 individual interviews with faculty members were undertaken by using a validated semi-structured interview guide. The interviews were recorded and transcribed verbatim. The thematic analysis of the data was done where codes were developed and arranged in different categories giving rise to discrete themes. Data triangulation from students and faculty results was done for convergence and correspondence to increase the credibility and authenticity of the study.

Results: Out of 24 students and 10 faculty members, half of the participants were females who shared their perceptions about gender bias in medical education. The analysis revealed 30 codes that were labeled and collated into 9 categories. The themes deducted from these categories were Lack of awareness, discriminatory attitude, the societal projection of the phenomenon, and the gendered climate in medical education.

Conclusion: Most of the students are not aware of the concept of gender bias. The study emphasizes that bias is a natural phenomenon but society and culture multiply the effect of this phenomenon. Most of the participants do believe that the assessment environment is made more comfortable and positive for female students. The study also revealed that gendered cultures of learning and assessment still exist in Gynaecology/Obstetrics and General Surgery departments.

Keywords: Gender bias, Assessment, Undergraduate Medical Education.

This article may be cited as: Aliya B, Jamil B, Ahmed F, Kashif L. Gender bias during assessments in undergraduate medical education: a qualitative study. J Med Sci 2022 July;30(3):222-226

INTRODUCTION

The general perception of medical institutions is that these are prodigious places where students get high-level academic knowledge, skills, and behaviors focusing on justice, respect, and equality.[1] The teaching environment plays an important role in learning and developing a positive professional identity. These learning perspectives significantly influence the graduates` beliefs and attitudes in their future professional and personal life.[2]

Any educational system needs to evaluate each student's performance objectively and without bias. Any discriminatory action may have a long-term impact on the personal and professional development of the future generation.[3] In educational research, a broad range of variables have been established that affect the teachers` judgment of student evaluation, including age, race, gender, ethnicity, financial status, and physical attractiveness. But society also holds stereotypic assumptions regarding boys' and girls' academic strengths and weaknesses.[4]

A significant change has been observed in the gender composition of medical institutes in the last few decades. It is becoming increasingly important as the number of women enrolled in medical Schools rises every year. Female representation accounts for more than half of the applicants in American and Canadian Medical schools, since 2002.[5] Similarly, in Pakistan, female representation is nearly sixty-five percent of registered medical college students, with the numbers increasing every year.[6]

Undergraduate medical students are very much exposed to discrimination, bias, and harassment as being at the bottom of the hierocracy of the medical profession.[4]

Correspondence
Dr. Lubna Kashif
Assistant Professor
Department of Medical Education Khyber Medical College, Peshawar - Pakistan
Cell: +92-321-9179191
Email: lubna148@live.ie
Date Received: 27-07-2022
Date Revised: 11-09-2022
Date Accepted: 27-09-2022

So, the establishment of a secure, unbiased environment should be a primary objective for all medical institutions.[5] Medical educators must realize the existing gender disparities in medical institutions to improve the curriculum, assessment, and training that can produce the top potential medical professionals.[7] Medicine is gender blind, and so should medical education.[8] The concept of gender bias within medical education has gained significant attention, though valid and reliable trials are needed to observe and report this phenomenon. [9] There has been inadequate data on gender discrimination in humanities generally and particularly in medicine. Previously, research has been conducted on the different subjects of gender discrimination as bullying, harassment, low career, and research opportunities for female medical students, including in Pakistan, but very few studies have been carried out to assess the prevalence of gender bias in undergraduate medical students` assessment.[4]

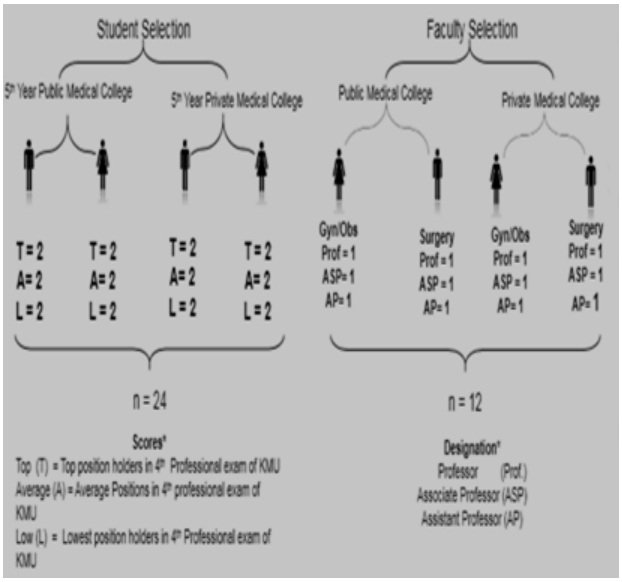

Fig 1: Sampling Method

MATERIALS AND METHODS

The study was conducted at a Public and Private Medical College in Peshawar, Pakistan, from June 2020 to October 2020. A qualitative research design with a phenomenological approach was employed. This study included year 5 MBBS students and faculty with more than 2 years of teaching experience. Participants were purposively selected through the maximum variation sampling technique. Data was collected through four focused group Interviews with year 5 medical students and ten individual interviews with faculty as there was no Assistant Professor available in the Surgery and Gynaecology/Obstetrics departments of the Private Medical College see Fig 1. A semi-structured interview guide was developed and validated by subject experts and a pilot study was carried out. Consent from the participants was obtained and anonymity and confidentiality were ensured. The interviews were recorded (via cell phone) and transcribed verbatim. The thematic analysis of the data was done by Braun & Clarke method. [10]

RESULTS

Out of 24 students and 10 faculty members, half of the participants were females who shared their perceptions about gender bias in medical education. The analysis revealed 30 codes that were labeled and collated into 9 categories. The themes deducted from these categories were Lack of awareness, discriminatory attitude, the societal projection of the phenomenon, and the gendered climate in medical education as shown in fig 2.

DISCUSSION

The primary focus of this qualitative research was to highlight the gender issues in assessing undergraduate medical students. Gender is a sociocultural construct and is a much-discussed psychological issue. This social con-

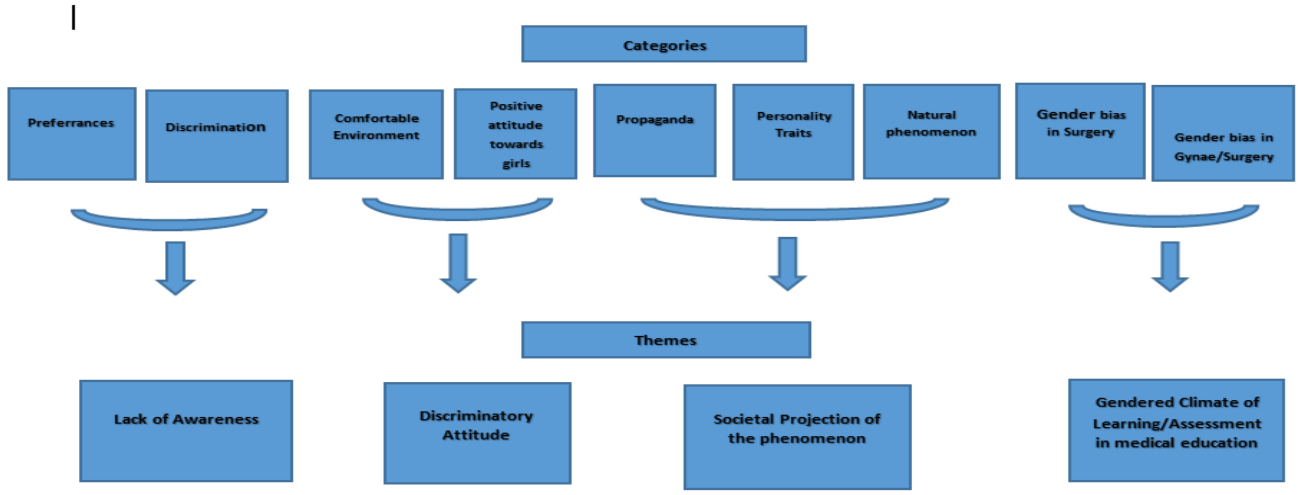

Fig 2: Thematic Analysis of the Data

struct changes continuously over time and varies across different cultures.[11, 12]We live in a sociocultural context, so prevailing social stereotypes influence our perceptions and opinions. It is not easy to isolate yourself from the influence of society as people generally don't readily accept challenges and strive for change.[13, 14] Over the last few decades, a significant decline has been observed in gender prejudice, particularly among cultured societies. However, still, these unconscious gender biases are exhibited in communities even by egalitarian individuals.[15]

The majority of the student participants did not apprehend the concept of sex and gender. They didn't comprehend the concept of gender bias. The only perception inculcated in their mind was that preference is given to girls irrespective of their capabilities and aptitude in the educational environment.

"… preference to a female based on the gender ideology rather than based on merit…."

This study highlighted that the assessment environment was made more comfortable and positive for girls as compared to boys. The male students also presumed that female students' physical appearance and personality traits helped them get higher grades. The girls did not have such apprehensions for boys, and they believed that this concept of favoring female students in academics is ingrained in society. Whereas the senior faculty didn't believe in gender bias in assessing undergraduate medical students. However, the junior faculty still believed that gender bias does exist in undergraduate medical education. This difference of opinion among senior and junior faculty reflected that age and professional maturity do have an impact on such sensitive issues.

One participant expressed, ***"In our community, there is a functional division between male and female. People don't understand the phenomenon of gender and sex. They take it as the same. But I think there is clear discrimination between males and females in undergraduate education."***

The male students comprehended that girls were usually assessed in a more comfortable environment by male assessors. In contrast, faculty behavior towards boys was stern and firm. One participant commented, ***"Male teachers make the examination environment comfortable for females but we get marks so it does not bother us so much. Mam, I don't agree that marks are unfair. I got deserving marks. But if examination environment becomes friendly for us too. We could perform better."***

As far as the personal experiences of gender bias, few students including, boys and girls, had experienced such discrimination during undergraduate medical education but most of the students perceived this phenomenon that female students get more marks from their colleagues and senior students. One student commented, ***"I have not experienced it myself. Boys always complain of this bias because this concept is inculcated in their minds. It exists in our culture. It has been inculcated in their minds that females get more marks."***

Whereas faculty believed that attraction towards the opposite gender is a natural phenomenon, it usually did not affect the assessment process. The majority of the participants perceived that our social context had a major role in creating this perception, ***"I accept this bias as a natural phenomenon. But the culture, especially our culture, multiplies the effect of this phenomenon"***

Wiskin et al. investigated the possibility of gender bias in a valid oral interactive contextualized examination of undergraduate final year medical students. They discovered that female students outperformed male students across the field in all stations, which had a minor but significant impact on their overall academic achievement.[11]

Ozlem Midik et al. found the same perception among undergraduate medical students in their study. According to this study, the majority of the male students presumed that gender had a significant impact on examination success. The male students firmly believed that female students used their sexuality to pass classes.[15] Another study by Thomas Delahuntthis et al. suggested that the perception of gender bias was due to typical gender stereotyping and gender schemas prevalent in society regarding female academic achievement. The psychologists identified that stereotypical labels had an essential role in developing specific schema and perceptions about any social phenomenon.[16]

D. Atyana and S. Olga also reflected on the correlation between beauty and advantage during college grades in their study and estimated that there were no significant relationships between college scores and attractiveness.[17]

The majority of the students reflected a gendered culture of learning in the surgery and Gynaecology/Obstetrics department in this study. These students described their personal experiences regarding learning and assessment based on gender in these two departments. The faculty did not believe in the gendered culture of learning and assessment in the Surgery and Gynaecology/Obstetrics departments because of the reforms in medical education and structured examination pattern.

One student expressed her views as, ***"…being a female, you should know it. I think knowledge expectation from females about Gynaecology is more as compared to male students. Similarly, junior and senior faculty guide us that Surgery is a male-dominated domain. Females cannot perform well in this field. We have been given different examples that females can't perform in this domain. ……. Think it over."***

In contrast, the faculty felt that the gendered culture in Surgery and Gynaecology/Obstetrics had declined due to medical education reforms and structured examination patterns. One respondent commented, ***"… in TOACS, every student has to perform. So, we expect from both genders in these specialties."***

Mimi Deng et al. assessed female medical students' knowledge, attitude, and practices regarding gender discrimination in Surgery by using a psychometric survey instrument in their study and discovered a highly prevailing perception of male dominance in Surgery among medical students.[18]

Ozlem Midik et al. reported in their study that most female student participants communicated that Surgery was more suitable for male students and females could not do Surgery, and College administrators intended to see more male students in Surgery.[15]

Akmal Z. Mohd Zahid et al. highlighted the gendered learning culture in the Gynaecology/Obstetrics clinical setting. Their study showed that male students acquired inadequate learning experience in Gynaecology/Obstetrics clinical setting and experienced higher levels of discrimination by teachers in the Gynaecology/Obstetrics department. This study proposed to reduce educational discrimination experienced by boys in undergraduate medical education to improve their learning opportunities in Gynaecology/Obstetrics domain.[19]

This study has established helpful information on the perceptions of gender bias in our educational environment but due to the subjectivity of the phenomenon, this study should be replicated in other medical institutes of the province in a different context to have a broader vision of this phenomenon that would help the medical institutes and educationists to devise the mechanism to counteract this issue.

CONCLUSION

Most of the students are not aware of the concept of gender bias as they perceived it as preferring female students in grading during assessment based on their physical attractiveness. The study emphasizes that bias is a natural phenomenon but society and culture multiply the effect of this phenomenon. Furthermore, these gender-specific concepts, beliefs, and perceptions are supported and communicated by society. Most of the participants do believe that the assessment environment is made more comfortable and positive towards female students which promotes this concept of favoring female students in assessments. The study also revealed that gendered culture of learning and assessment still exists in the Gynaecology/Obstetrics and Surgery domains of medical education.

REFERENCES

1. Kumari R. Gender Disparity in Medical Education : An Analysis of Gender Exclusion and Discrimination among the Social Groups. 2019;10(6):446–54.
2. Selic P, Cerne A, Klemenc-Ketis Z, Petek D, Svab I. Attitudes toward professionalism in medical students and its associations with personal characteristics and values: What actually makes a difference? [Response to the letter]. Adv Med Educ Pract. 2019;10:689–92.
3. Dacre J. Are there too many female medical graduates? No. BMJ. 2008;336(7647):749.
4. Hashmi AM, Rehman A, Butt Z, Aftab MA, Shahid A, Khan SA. Gender discrimination among medical students in Pakistan: A cross-sectional survey. Pakistan J Med Sci. 2013;29(2):449–53.
5. Islam KM, Asadullah MN. Gender stereotypes and education: A comparative content analysis of Malaysian, Indonesian, Pakistani and Bangladeshi school textbooks. PLoS One. 2018;13(1):1–24.
6. Birch P, Batten J, Batey J. The influence of student gender on the assessment of undergraduate student work. Assess Eval High Educ. 2016;41(7):1065–80. Available from: http://dx.doi.org/10.1080/02602938.2015.1064857
7. Morgan AU, Chaiyachati KH, Weissman GE, Liao JM. Eliminating Gender-Based Bias in Academic Medicine: More Than Naming the "Elephant in the Room." J Gen Intern Med. 2018;33(6):966–8.
8. Parker RB, Parker PD, Larkin T, Cockburn J. A psychometric evaluation of the Gender Bias in Medical Education Scale. BMC Med Educ. 2016;16(1):1–9. Available from: http://dx.doi.org/10.1186/s12909-016-0774-2
9. Brown MEL, Hunt GEG, Hughes F, Finn GM. Too male, too pale, too stale: A qualitative exploration of student experiences of gender bias within medical education. BMJ Open. 2020;10(8):1–14.
10. Kiger ME, Varpio L. Medical Teacher Thematic analysis of qualitative data: AMEE Guide No. 131 Thematic analysis of qualitative data: AMEE Guide No. 131. [cited 2022 Aug 18]; Available from: https://doi.org/10.1080/0142159X.2020.1755030
11. Wiskin CMD, Allan TF, Skelton JR. Gender as a variable in the assessment of final year degree-level communication skills. Med Educ. 2004;129–37.
12. Hare-Mustin, Rachel T.; Marecek J. Gender and the Meaning of Difference: Alpha and Bata Bias.
13. Babaria P, Abedin S, Berg D, Nunez-Smith M. "I'm too used to it": A longitudinal qualitative study of third-year female medical students' experiences of gendered encounters in medical education. Soc Sci Med. 2012;74(7):1013–20. Available from: http://dx.doi.org/10.1016/j.socscimed.2011.11.043
14. Moss-Racusin CA, Dovidio JF, Brescoll VL, Graham MJ, Handelsman J. Science faculty's subtle gender biases favor male students. Proc Natl Acad Sci U S A. 2012;109(41):16474–9.
15. Midik Ozlem, AytuĞ KoŞan AM, Coskun O, Baykan

Z, SÜrel Karabilgin ÖztÜrkÇÜ Ö, Şenol Y. Gender in Medical Education in Turkey: The Intern Perspective. J Adv Med Educ Prof. 2020;8(4):149–57.

16. Kollmayer M, Schober B, Spiel C. Gender stereotypes in education: Development, consequences, and interventions. Eur J Dev Psychol. 2018;15(4):361–77. Available from: http://dx.doi.org/10.1080/17405629.2016.1193483
17. Deryugina T, Shurchkov O. Does beauty matter in undergraduate education? Econ Inq. 2015;53(2):940–61.
18. Deng M, Nham E, Malvea A, Ramsay T, Seabrook C, Watterson J. Exploring the Impact of the Surgical Exploration and Discovery (SEAD) Program on Medical Students' Perceptions of Gender Biases in Surgery: A Mixed-Method Evaluation. J Surg Educ [Internet]. 2021;78(4):1236–49. Available from: https://doi.org/10.1016/j.jsurg.2020.11.016
19. Zahid M,Akmal Z, Ismail Z, Abdullah B, Daud S. Gender bias in the training of medical students in obstetrics and gynecology: A myth or reality? Eur J Obstet Gynecol Reprod Biol. 2015;186:17–21. Available from: http://dx.doi.org/10.1016/j.ejogrb.2014.12.018

CONFLICT OF INTEREST: Authors declare no conflict of interest

GRANT SUPPORT AND FINANCIAL DISCLOSURE: NIL

AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under

Aliya B: Concept, Design, and Proofreading

Jamil B: Acquisition and critical review

Ahmed F: Analysis and interpretation of data

Kashif L: Review and writing

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

LAURENCE-MOON-BARDET-BIEDL SYNDROME: A CASE REPORT

Nayab Munib[1], Iqbal Haider[1], Suleman Elahi[2]

Department of Medicine, MTI Khyber Teaching Hospital, Peshawar - Pakistan

Division of Diabetes and Endocrinology, Khyber Teaching Hospital, Peshawar - Pakistan

This article may be cited as: Munib N, Haider I, Elahi S. Laurence-moon-bardet-biedl syndrome: a case report. J Med Sci 2022 July;30(3):227-229

INTRODUCTION

Laurence-Moon-Bardet-Biedl Syndrome (LMBBS) is a rare autosomal recessive innate disorder, ensuing as a result of consanguineous marriage. It characteristically manifests as a congenital ciliopathy with a saga of widely distinct primary and secondary clinical features. Patients with LMBBS experience rapid decline in the functionality of the brain, eyes, kidneys, hands, and feet. The cardinal features typical of the syndrome include mental retardation, atypical retinitis pigmentosa, hypogonadism, polydactyly, obesity, and renal impairment.

Nonetheless, it may also present with certain secondary characteristics including speech disorders, gait disturbances, developmental delay in achieving milestones, diabetes insipidus, syndactyly, dental crowding or hypodontia, and congenital heart disease. Renal impairment is also a frequent clinical manifestation. Such patients are confused, along with impeded memory, poor judgment skills, and uncoordinated, and clumsy motor movements. While renal impairment remains the major cause of mortality since end-stage renal disease is a frequent complication in such patients; overall, LMBBS is a rare syndrome of multi-organ involvement with various degrees of complications and an uneven life span [1].

CASE PRESENTATION

A 13 years old female patient presented to the general medicine outpatient department (OPD) with the chief complaints of obesity, learning difficulty, polyuria, polydipsia, and gradual loss of vision since childhood followed by night blindness. Detailed history revealed that she was the fifth child of consanguineous marriage, born full term at home in a village. Bilateral polydactyly and syndactyly were observed since birth, however, she started to gain weight in infancy. The patient demonstrated delayed milestones compared to her siblings evidenced by the fact that she took her first step at the age of 4 years. Moreover, the patient is neither able to read or write properly nor could she retain the things she has learned the past day. The patient further elaborated on her ailment that she is unable to see during the night and has near to complete vision during the day. Probing into the family history revealed that one of her brother age 8 years also has the same clinical features while the remaining eight siblings were normal.

On general physical examination, she had marked obesity with a BMI of 38 kg/m2 and a moon-like face (fig 1). Polysyndactyly was noted in both hands along with polydactyl of the right foot (fig 2,). There was a lack of pubic and axillary hair. Central Nervous Examination revealed a wide-based stance while walking and an inability to recall even the simplest information like where does she live? Abdominal examination revealed a soft, distended, non-tender abdomen with grayish striae. Respiratory and cardiovascular examinations were unremarkable. Ultrasound of the abdomen and pelvis showed grade 2 fatty liver and mildly increased left renal echogenicity. Eye examination revealed color vision defect on Ishihara color chart and reduced visual acuity of 6/24 in both eyes. The Hiding Heidi Test showed a 25% decreased vision perception. Laboratory investigations revealed normal full blood count, C-reactive protein (CRP), renal function test, liver function test, lipid profile, and thyroid function test. However, her follicular stimulation hormone (FSH) and luteinizing hormone (LH) were below the normal level. As this patient met the criteria for the diagnosis of LMBBS, the diagnosis of LMBBS was made, a multidisciplinary team (MDT) was taken on board and the treatment was focused on managing symptoms. Ophthalmic support, hormone therapy, and speech and occupational therapy were recommended. The patient was sent out on multivitamins and supplements and the parents were counseled regarding the nature, course, and poor prognosis of the disease.

Correspondence
Dr. Iqbal Haider
Associate Professor
Department of Medicine, Khyber Teaching Hospital,
Peshawar - Pakistan
Email: driqbalhaiderkth@gmail.com
Cell: +92-313-9696102
Date Received: 13-09-2022
Date Revised: 28-09-2022
Date Accepted: 28-09-2022

DISCUSSION

LMBBS is a heterogeneous disorder with familial occurrence manifesting various clinical features that results in a complex association of problems affecting several body parts. It was named after the four scientists who initially described the symptoms. Although LMBBS is considered a single entity, it comprises two distinct syndromes i.e. Laurence Moon Syndrome (LMS) and Bardet Beidl Syndrome (BBS). Both are genetically inherited in an autosomal recessive pattern. However, LMS has an atypical pigmented retinopathy along with hypogonadism, neurological defects, and mental retardation but no polydactyly or obesity which are the cornerstones of the BBS. Nonetheless, the symptoms of LMBBS are obvious, yet it remains an underdiagnosed condition. It predominantly affects females and has the occurrence of 1:140000 to 1:160000 in North America and Europe respectively, while greater

The occurrence was reported in Kuwait and Newfoundland, having 1:13500 to 1:17500 respectively[2]. The patient described in this case report is a typical representation of LMBBS. Genetic testing to date has revealed 19 culprit genes associated with the disease, all of which encode protein cilia. LMS is caused by changes in PNLP6 genes whereas BBS results from mutations in at least 14 different BBS genes. About one-quarter of all cases of Bardet-Biedl syndrome

results from mutations in the BBS1 gene. Another 20 percent of cases are caused by mutations in the BBS10 gene. The other BBS genes each account for only a small percentage of all cases of this condition [3]. Both parents need to carry one copy of the mutated gene for the child to develop LMBBS. The first prime feature of LMBBS is retinal dystrophy and vision loss which often ensues due to impaired photoreceptors in retinal tissue involving macula leading initially to night blindness, followed by complete blindness over course of time. It is usually observed in the first decade of life in few people and observed by all in the second decade.

Another important feature of LMBBS, obesity, begins in childhood and progresses as the patient ages with a frequency of 72-96 % as determined by the measurement criteria. The average body mass index (BMI) reported in female patients is 31.5 kg/m2, while in male patients is 36.6kg/m2 [4,5]. Skeletal abnormalities particularly polydactyly and syndactyly are another main feature of this syndrome with polydactyly usually occurring in 69% of LMBBS patients [6]. people with LMBBS often have decreased levels of sex hormones estrogen and testosterone mainly due to the small size of the pituitary gland. As a result of a weak signal to produce estrogen and testosterone, the reproductive organs of both men and women suffering from LMBBS may be underdeveloped resulting in reduced fertility or sometimes even infertility. Mental sub normality is a borderline manifestation of this syndrome. It is debatable but most patients have lower IQ with learning disabilities attributed to weak cognitive capacity. The patient under discussion presented with all five aforementioned symptoms. A study carried out by Beales et al. on 109 BBS patients devised a modified diagnostic criterion[7]. According to the criteria, an individual must have at least four primary features or three primary and two secondary features to be identified as BBS patient. [Table 1]

Another main feature associated with LMBBS is a renal impairment which is a leading cause of mortality. Impaired urinary concentration capacity, recurrent urinary tract infections, and hypertension are early presentations. There are several renal abnormalities detected including dysplastic kidneys, parenchymal cyst, calyceal clubbing, and chronic renal failure. Typical radiographic pictures are seen in these patients.

LMBBS requires a multidisciplinary approach and an early diagnosis to ensure the quality of life. Counseling regarding hereditary nature, the risk of the disease, and creating awareness regarding consanguineous marriage can reduce the prevalence of the disease. Furthermore, early detection of the disease can significantly reduce the advancement of manifestations. Treatment options at a later stage mostly comprise supportive treatment. Spectacles and visual aids have been advised to improve visual quality; physical exercise and a low-calorie diet are the mainstream treatment to reduce obesity. Moreover, hormonal therapy can improve hypogonadism to some extent. Additionally, in order to slow down the cognitive impairment, educational evaluation should be performed and analyzed by a clinical psychologist who can also counter the mood symptoms if produced as a consequence of this disease [8].

Fig 1: Karyotyping revealed a genotype of 46 XY.

Fig 2: Polysyndactyly.

CONCLUSION

LMBBS, a rare genetic disorder, imposes considerable morbidity and mortality. As there is no definite treatment to date, early diagnosis is essential to manage the complications related to this condition like retinitis pigmentosa, morbid obesity, and metabolic syndrome. A multidisciplinary evaluation approach involving physicians, ophthalmologists, endocrinologists, pediatricians, and radiologists can significantly alter the course of the disease, enabling the affected individuals to integrate better into the community. Consanguineous marriages being an effective contributor to LMBBS need particular attention. In this scenario, marriages outside of the family should be encouraged to limit the incidence. As the disease carries a lot of morbidities, genetic study and genetic counseling are mandatory for patients with suspicion of LMBBS.

REFERENCES

1. Forsyth RL, Gunay-Aygun M. GeneReviews®. Seattle: University of Washington; 2003. Bardet-Biedl syndrome overview. [Google Scholar]
2. Hypokalemic paralysis and megaloblastic anaemia in Laurence-Moon-Bardet-Biedl syndrome. Abbasi A, Butt N, Sultan B, Munir SM. J Coll Physicians Surg Pak. 2009;19:186–188. [PubMed] [Google Scholar]
3. Beales PL, Badano JL, Ross AJ, Ansley SJ, Hoskins BE, Kirsten B, Mein CA, Froguel P, Scambler PJ, Lewis RA, Lupski JR, Katsanis N. Genetic interaction of BBS1 mutations with alleles at other BBS loci can result in non-Mendelian Bardet-Biedl syndrome. Am J Hum Genet. 2003 May;72(5):1187-99. Epub 2003 Apr 3. Citation on PubMed or Free article on PubMed Central
4. Bardet-Biedl syndrome. Forsythe E, Beales PL. Eur J Hum Genet. 2013;21:8–13. [PMC free article] [PubMed] [Google Scholar]
5. Clinical and genetic epidemiology of Bardet-Biedl syndrome in Newfoundland: a 22- year prospective, population-based, cohort study. Moore SJ, Green JS, Fan Y, et al. Am J Med Genet A. 2005;132:352–360. [PMC free article] [PubMed] [Google Scholar]
6. BBS genotype-phenotype assessment of a multiethnic patient cohort calls for a revision of the disease definition. Deveault C, Billingsley G, Duncan JL, et al. Hum Mutat. 2011;32:610–619. [PubMed] [Google Scholar]
7. New criteria for improved diagnosis of Bardet-Biedl syndrome: results of a population survey. Beales PL, Elcioglu N, Woolf AS, Parker D, Flinter FA. J Med Genet. 1999;36:437–446. [PMC free article] [PubMed] [Google Scholar]
8. Bardet-Biedl syndrome. Forsythe E, Beales P. Eur J Hum Genet. 2013;21:8–13. [PMC free article] [PubMed] [Google Scholar

CONFLICT OF INTEREST: Authors declare no conflict of interest

GRANT SUPPORT AND FINANCIAL DISCLOSURE: NIL

AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under

Munib N:	Did literature search, article formatting, and compilation
Haider I:	Conceived the idea, final review
Elahi S:	Article formatting, and compilation

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

INSTRUCTIONS FOR AUTHORS

Manuscript Submission

The Journal of Medical Sciences follows the uniform requirements for manuscripts submitted to Biomedical Journals as approved by the International Committee of Medical journal Editors as updated in Oct. 2004 and available at www:icmje.org. Manuscripts are accepted for consideration if neither the article nor any of its contents has been or will be published or submitted elsewhere before appearing in Journal of Medical Sciences.

Manuscript Formatting Guideline

While submitting the document on JMS website, the authors are advised to follow the following guidelines:

1) Always use MS Word format. Don't send any tables in JPG format.

2) Always use Calibri fonts.

3) use 12 size fonts.

4) Double space the manuscript.

5) Justify the margins

6) Keep the main headings bold and in size 14.

7) No extra spaces between paragraphs.

8) Black text on white background only.

Title and Authors Name

The first page of the manuscript must give the title of the article that should be concise and descriptive. Also include on this page the name(s) of the author(s), highest academic degrees, the name of the department and institution in which the work was done, the institutional affiliation of each author, and the name and address of the author to whom reprint requests should be addressed.

Any grant/support that requires acknowledgement should be mentioned on this page. Abstract's word count and article (excluding references) word count should appear at the bottom of this page.

Abstracts

Abstract must not exceed 250 words and the **article must not exceed 3000 words** (excluding references). Articles exceeding the word count or not conforming to "Instructions for authors" will be returned without processing. It is further emphasized that results must not be duplicated in text/tables/figures/graphs.

Key words

Three to 10 key words or short phrases should be added to the bottom of the abstract page. Terms from the Medical subject headings (MeSH) list of Index Medicus should be used.

Introduction, Material and Methods, Results, Discussion, Conclusion, Acknowledgments and references should all start on a separate page from page 03 onwards.

References

The total number of references in an original article must not exceed 40 while in the review articles maximum limit is 100. References must be written double-spaced and numbered as they are cited in the text.

The references must be written in Vancouver style. The style for all the types of references is given in the "Uniform requirements for manuscripts submitted to biomedical journals" at the website of International Committee of medical journal editors. **www.icmje.org**

List all authors when there are six or fewer. If there are more than six, list the first six followed by "et al".

Tables and Illustrations

Each of the tables and illustrations should be on a separate page, must have a title and be on a double space.

Figures should be professionally designed. Symbols, lettering and numbering should be clear and large enough to remain legible after the figure has been reduced to fit the width of a single column. The back of each figure should include the sequence number, the name of the author and the proper orientation (e.g. "top"). If photographs of patients are used, either the subjects should be unidentifiable or their pictures must be accompanied by written permission to use the figure. Duplication of results given in tables and into figures must be avoided.

Ethics

When reporting experiments on human subjects, indicate whether the procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (Institutional or regional) and with the Helsinki Declaration of 1975, as revised in 1983. Do not use patients names, initials, or hospital numbers especially in illustrative material. When reporting experiments on

animals, indicate whether the institution's or a national research council is guide for, or any national law on the case and use of laboratory animals was followed. No article will be entertained without prior ethical approval from ethics committee/ board.

Units of Measurements

Authors should express all measurements in conventional units, with System International (SI) units given in parentheses throughout the text.

Abbreviations

Except for units of measurements abbreviations are discouraged. The first time an abbreviation appears it should be preceded by the words for which it stands. However title and abstract must not contain any abbreviation.

Statistics

Describe statistical methods with enough detail to enable a knowledgeable reader with access to the original data to verify the reported results. When possible quantify findings and present them with appropriate indicators of measurements error or uncertainty (such as confidence intervals). Avoid relying solely on statistical hypothesis testing, such as the use of ρ values, which fails to convey important quantitative information. Discuss the eligibility of experimental subjects. Describe the methods for and success of any binding of observations. Report complications of treatment. Give numbers of observations. Report losses to observation (such as dropouts from a clinical trial). Specify any computer programs used.

Put a general description of methods in the Methods Section. When data is summarised in the Results Section, specify the statistical methods used to analyse it. Restrict tables and figures to those needed to explain the argument of the paper and to assess its support avoid non technical uses of technical terms in statistics, such as "random" (which implies a randomizing device) "normal" significant, "correlation", and sample.

Define statistical terms, abbreviations, and most symbols.

Drug Names

Only generic names should be used.

Permissions

Materials taken from other sources must be accompanied by a written statement from both author an publisher giving permission to the journal for reproduction.

Case Report

Short report of cases, clinical experience, drug trials or adverse effects may be submitted. They must not exceed 500 words, 5 bibliographic references and one table or illustration. The report must contain genuinely new information. The format is title, abstract, introduction, case report, discussion, references.

Review and Action

All articles on receipt for publication are immediately acknowledged but that does not imply acceptance for publication.

Submitted manuscripts are reviewed for originality, relevance, statistical methods, significance, adequacy of documentation, reader interest and composition. Manuscripts not submitted according to the instructions will be returned to the author for correction prior to beginning the peer review process. All manuscripts considered suitable for review are evaluated by a minimum of two members of editorial board. The manuscripts is then sent to two or more than two reviewers who may take a couple of months time to review the manuscript. The ultimate authority to accept or reject the manuscript rests with the Editor.

Revised manuscripts are judged on the adequacy of responses to suggestions and criticisms made during the initial review. All accepted manuscripts are subject to editing for scientific accuracy and clarity by the office of the Editor. When the manuscripts is deemed fit for publication, letter of acceptance is issued to the author. No article is rejected unless similar comments are received from at least two reviewers.

FOR DETAILS, SEE OUR EDITORIAL POLICY IN THE NEXT SECTIONS

AUTHOR'S AGREEMENT

Journal of Medical Sciences (KMC Peshawar pISSN 1997-3438)

ArticleTitle_____

The undersigned author (after reviewing criteria for authorship as defined by International Committee of Medical Journal Editors [ICJME] found at 'http://www/icmje.org/' and have participated reasonably in the intellectual content, analysis of data and writing of the article) jointly and severally, hereby transfer and assign all rights, title, and interest therein, including any and all copyrights in all forms and media now or hereafter known, to the Journal of Medical sciences. The author/s retain the nonexclusive right to use part or all of the article in future work of their own, provided proper credit is given to the Journal of Medical Sciences. In case, the submitted article is not published, the Editorial Board agrees to release its rights therein.

I certify that

A) None of the material in the manuscript has been published previously/currently under consideration for publication elsewhere.

B) The article has not been accepted for publication elsewhere

C) I have not signed any right or interest in the article to any third party

D) I am able/willing to produce the data on which this article is based, should the Editorial Board of the Journal of Medical Sciences request such data.

E) Animal Care Committee/Institutional Review Board approval was granted for this study.

I (including spouse and children), disclose financial interest at the level

a) Nothing to disclose b) Financial interest to the amount of _____

F) I/We confirm to comply fully with the suggestions/critical views of the reviewers/editor, failing which my/our article may be rejected at the sole discretion of the editor. I/we further confirm that if our article is rejected (whihc is the sole discretion of the editor) I/we will have no right to complain against the journal/editor/ representative of the journal/printer in any forum including the court of law.

G) I/we suggest the following two overseas reviewers to review our article.

1) _____	_____	_____
2) _____	_____	_____
Name of reviewer	Postal address	Email address & Telephone No.

_____	_____	_____
Author name	Author signature	Author e-mail address

Note: Author agreement form must be signed by each author (one page for each) and submitted with the article.

Author's Checklist:

i) Eliminate nonstandard abbreviation in the titles
ii) Supply full author names (including institutional affiliation and contact informations)
iii) Contribution of individual authors
iv) Nomination of first 3 co-authors by the principal author
v) Abstract: 200 words, Article: 2000 words (excluding references).
vi) Supply references in Vancouver style, accurately cited in the text in numerical order
vii) Cite tables in the text in numerical order
viii) Send 03 Hard copies and on a R/W CD (in MS Word), in a protective envelop, do not use clips
ix) Cite figures in the text in numerical order
x) Author agreement is signed by all authors.
xi) Departmental Permission Letter for the study.
xii) Letter of ethical review of concerned hospital/study place.
xiii) Bank draft for Rs. 5000/- (Rs. Five Thousand) in the name of Journal of Medical Sciences, Peshawar, Pakistan/or deposit in cash with Managing Editor Account No. 4048685170 (3548-9) Can be transferred ONLINE to the Account No. 4048685170 (3548-9) Branch Code 0388 at National Bank of Pakistan, University Campus Branch, Peshawar.

EDITORIAL POLICY

EDITORIAL POLICY OF JOURNAL OF MEDICAL SCIENCES (JMS), KHYBER MEDICAL COLLEGE, PESHAWAR

OVERVIEW

This document highlights the mission, objectives and editorial policy of JMS in regard to publication process by adhering to the guidelines by COPE (Committee in Publication Ethics) and ICMJE (International Committee of Medical Journals Editors). Each component of the editorial policy is explained in the next sections.

A MISSION OF JMS

To publish relevant, scientific and accessible material to help medical students and health professionals in their practice, teaching and learning, and career development

B OBJECTIVES OF JMS

a To publish clinical, epidemiological, public health, educational, translational, and allied sciences research to enable the scientists, clinicians and researchers to learn about developments and innovations in these disciplines

b To publish high quality descriptive and experimental research, review articles, editorials and case reports to enhance the understanding of scientific community regarding clinical practice and education

c To provide a platform for scientific community in promoting their career development through publishing quality research

C EDITORIAL POLICY

1 Open access

JJMS is an Open access scholarly literature source that is free of charge and often carries less restrictive copyright and licensing barriers than traditionally published works, for both the users and the authors. However, it complies with well-established peer review processes and tries to maintain high publishing standards.

2 Peer review process

The review process of JMS is following a "triage approach". Upon submission of a manuscript, either online or physical, the document undergoes a preliminary open (un-blinded) review in the office of the chief editor. The document is either accepted for further review, sent for revision back to the authors, or rejected at that time. Further review of JMS is following a blinded approach, where the article is sent to 2 reviewers, a local and international. During this process, all the relevant information about the authors and reviewers is kept confidential. However, we encourage to share reviewers' comments with co-reviewers of the same paper in a blinded manner, so reviewers can learn from each other in the review process. We also encourage the readers to send us the post publication reviews about a research work in the form of letters to the editors, which are then published and shared with the authors of relevant articles. The editorial board has the authority to retract an article if serious violation of credibility or quality of research is found after the article is published.

The journal is under no obligation to send submitted manuscripts for review, and under no obligation to follow reviewer recommendations, favourable or negative at all times. The editor of a journal is ultimately responsible for the selection of all its content, and editorial decisions may be taken by issues unrelated to the quality of a manuscript, such as suitability for the journal. An editor can reject any article at any time before publication, including after acceptance, if concerns arise about the integrity of the work.

3 Authorship

According to the ICMJE criteria, authorship is based on 4 criteria; (1) conceptualization and designing, (2) AND, data collection, (3) AND, writing and critical review, (4) AND, taking responsibility for the authenticity and integrity of all the research process. All those designated as authors should meet all these 4 criteria. The

co-authors should declare their roles and contributions in the research process explicitly. Those who do not meet all 4 criteria should be ACKNOWLEDGED only. If agreement cannot be reached about who qualifies for authorship, the institution(s) where the work was performed, not the journal editor, should be asked to investigate. If authors request removal, addition or change in the sequence of an author after manuscript submission or publication, journal editors should seek an explanation and signed statement of agreement for the requested change from all listed authors and from the author to be removed or added. The corresponding author is the one individual who takes primary responsibility for communication with the journal during the manuscript submission, peer review, and publication process. The corresponding author typically ensures that all the journal's administrative requirements, such as providing details of authorship, ethics committee approval, clinical trial registration documentation, and disclosures of relationships and activities, are properly completed and reported.

4 Submission of manuscript

The manuscript should be submitted through journal website which is using the Online Journal System (OJS) along with the Institution research and ethics board (IREB) certificate. The article should have the following format:

4.1: The abstract should be structured with word count of not more than 250 words.

4.2: The fonts should be Calibri, with size 12, and spacing of 1.5, with justified margins in MS office format.

4.3: The whole document should not be more than 3000 words (excluding references and appendices).

4.4: The number of figures and tables should not exceed 5 in the whole document.

4.5: The pictures and tables should be black and white in color.

4.6: Copied pictures and tables from other sources will not be entertained, unless a written approval from the original researcher and publisher is provided

5 Institutional research and Ethics board (IREB) certificate

Under no circumstances, an article will be accepted if approval from the relevant ethical board / committee is not taken before the start of a research. The board / committee should assess the proposal of a research in both ethical and technical aspects before giving a certificate of approval.

6 Conflict of interest

To ensure transparency in the research conduction, writing and publication, the authors, peer reviewers and editors have to declare conflicts of interest regarding financial aspects, academic competitions, and relationships during writing, reviewing and publishing the manuscripts. Details of sponsors along with their roles and access to data should be clearly stated.

7 Confidentiality

The editorial board in no way should publicize the work of a researcher in any form unless it is published. They should not publicize the comments and critique given by reviewers. Similarly, the reviewers are bound to keep the confidentiality of the work of researchers during and after the review. The work of researchers and the critique should never be discussed or exemplified in forums. The confidentiality of the researchers should be maintained in every possible way when the documents are sent for review. However, our review process is open (non-blinded) in the first phase, as per policy of the journal. In this case, the policy is clearly displayed on journal`s website for the researchers. Reviewers must not retain the manuscript for their personal use and should destroy paper copies of manuscripts and delete electronic copies after submitting their reviews. If a manuscript is rejected, it should be deleted from the editorial system. If an article is published, the manuscript along with its reviews and other relevant documents should be retained for a period of 3 years and then deleted. The only situation where confidentiality needs to be breached is when a situation of fraud or misconduct is found during the review process or after publication. Still, the authors and sometimes the reviewers, have to be notified.

8 Correction and retraction of articles

The guidelines for correction and retraction of articles are as follows:

8.1: A specific page is allocated in the journal (both electronic and printed) that will be used for news related to corrections in articles published in previous journals.

8.2: The editor should also post a new article version in the journal with details of the changes from the original version and the date(s) on which the changes were made.

8.3: Previous electronic versions will prominently note that there are more recent versions of the article (that will be placed at the end of abstract). Similarly, the more recent version should be cited by the authors or others.

8.4: If the error is judged to be unintentional, and the underlying science appears valid, and the changed version of the paper survives further review and editorial scrutiny, then retraction with republication of the changed paper, with an explanation, allows full correction of that research paper.

8.5: If serious violation of credibility or quality of a research paper is found after the publication, the article has to be retracted after approval of at least 3 members of the editorial board in consultation with chief editor. The whole process will follow the guidelines presented by Committee on publication ethics (COPE).

8.6: The retracted article should clearly be notified on the website and the word “retracted” should be mentioned along the title of the article.

9 Correspondence

Correspondence for submitting an article in JMS will be through a corresponding author. The duties of a corresponding author have already been presented in a previous section. Correspondence regarding debating an article is given high value and a separate page for letters to the editors has been allocated. Derogatory and demeaning letters are screened and letters which promote debates and critique are encouraged to be published. However, correspondence about the articles published in the last 1 year will be included only.

10 Fee submission process

The editorial board in a recent meeting has fixed a fee of 7000/- Rs (Pakistani), for local authors and 250 $ (US) for international authors. The fee should be submitted as bank draft/online payment through account (IBAN) no: PK56NBPA0388004048685170 (Branch code: 0388 / National Bank of Pakistan, University campus branch, Peshawar, Pakistan) as follows:

1) Article processing fee of 3000/- PKR at the time of submission of article after acceptance for preliminary / initial triage, open review by the Chief Editor. This amount will be non-refundable.

2) Article publication fee of 4000/- PKR at the time of acceptance of article after external review. This amount will be refundable if the article is rejected for any reason.

3) For international authors, the amount of 250 US dollars will be accepted after both internal and external review. Researchers belonging to countries other than Pakistan are advised to submit the fee after the whole process of review is completed and the article is accepted for publication.

11 Roles of editorial board, editors and members

The editorial board of JMS is following the Higher Education Commission (HEC) policy for research journals. The roles of the editorial board for JMS are mentioned below:

11.1: The roles of the Editorial Board are:

11.1.1: To offer expertise in their specialist area

11.1.2: To review submitted manuscripts

11.1.3: To advise on journal policy and scope

11.1.4: To work with the Editor to ensure ongoing development of the journal

11.1.5: To identify topics for special issues of the journal or recommend a Conference which would promote the journal, which they might also help to organize and/or guest edit

11.1.6: To attract new and established authors and articles

11.1.7: To submit some of their own work for consideration, ensuring that they adhere to Conflict of Interest rules and stating their relationship to the journal. This is very important as the journal cannot be seen to publish only papers from members of the Editorial Board.

11.1.8: It is important that Editorial Boards have a regular communication forum with other boards of similar nature, either face to face in person (depending on their country of origin, funding availability, etc.) or as more journals are doing today, communicating by teleconference, Skype or other web platforms.

11.2: The Patron:

The Patron is usually the Dean of the institute, and is overall incharge of the journal, who needs to be kept informed of the decisions taken by the editorial board. The patron is the final authority to approve the decisions and policies of the editorial board.

11.3: The Chief Editor:

11.3.1: The criteria for selection of Chief Editor are:

i. Expertise and experience in the specialist field related to the journal

ii. Publication record of a number of articles and /or books (usually in / related to the specialist field)

iii. Being a reviewer for an international peer reviewed journal

iv. Senior research position with equivalent experience in research and scholarship

v. Enthusiasm to undertake the Editor role

vi. Preferably a diploma, master or doctoral degree in Education and Research. It is not necessary to fulfill all the criteria to become a chief editor

11.3.2: The roles of Chief Editor are:

i. The key role of a journal`s chief editor is to promote scholarship in the specialist field associated with the journal, whilst also promoting the journal as the best journal to publish in. For any journal, the editor will need to encourage new and established authors to submit articles and set up a reliable panel of expert reviewers. Editors are also responsible for offering feedback to reviewers when required and ensure that any feedback to authors is constructive.

ii. An editor should also familiarize themselves with the Committee on Publication Ethics (COPE) 'Code of Conduct and Best Practice Guidelines for Journal Editors'.

iii. Depending on how the journal is managed and how it is structured, an Editor may have to make all the decisions regarding which articles to accept or reject for publication.

11.3.3: Managing editor:

The roles of manging editor are:

i. To help the chief editor to achieve the above-mentioned goals

ii. To communicate with the authors, reviewers, publishers and other agencies for smooth running of the journal

iii. To regularly evaluate the research work

iv. To communicate with funding and regulating agencies (HEC and others) for grants and accreditations.

11.3.4: Executive editor:

The roles of executive editor are:

i. To evaluate the research articles presented for publication

ii. To help the editorial board in policy making

iii. The help the editorial board in smooth publishing

iv. To communicate with reviewers and collaborate with external agencies for relevant purposes

11.3.5: Section editors:

Section editors are allotted different responsibilities. Some of these are mentioned below:

i. Bibliography

ii. Proof-reading

iii. Academic writing reviewing, grammar and spell checking

iv. Dissemination of articles for review

v. Contact with publishers under the supervision of senior editorial team

vi. Training of future reviewers, young members and other faculty members

vii. others

11.3.5: Editorial advisory board:

Editorial advisory board members consist of national and international senior academicians, researchers, clinicians and others to help the current editorial board in designing, implementing and evaluating policies regarding upgrading the quality of research work. These people also share best practices to help the editorial team to refine their research work.

12. POLICY REGARDING RECRUITMENT AND CONTINUATION OF EDITORIAL BOARD

Policy for recruitment and continuation of the editorial board is based on the guidelines discussed in the previous section. The chief editor, managing editor and executive editors are recruited by the patron in-Chief. Members are then selected by them from amongst the faculty who have an aptitude for research, and their names are endorsed by the patron. The tenure of editorial board is decided by the Patron after a period of 3 years whether to continue or recruit a new team or member. The editorial advisory board members are recruited for indefinite period by the editorial team of JMS.

13. Plagiarism policy

he journal is following the plagiarism policy of Higher Education Commission of Pakistan, and for this purpose, a plagiarism standing and review committee has been established under the chairmanship of Chief Editor of JMS along with 4 members amongst senior faculty. The committee has been given the authority to review research papers and plagiarism complaints related to published work in the journal.

14 Contact information

The office of managing editor or chief editor should be contacted anytime in working hours or can be contacted through their emails for correspondence.

REFERENCES

1. ICMJE recommendations
2. COPE guidelines
3. SCOPUS

This document is prepared in January 2020 to be used by editorial board, reviewers, researchers and faculty as a guide to make them aware of policies and procedures of publishing, conducting, writing, reviewing and evaluating the research published in JMS. This document is developed by including the recommendations of ICMJE (2019) and COPE guideline and in case of any conflict, lack of clarity and ambiguity, the recommendations of latest ICMJE recommendation and COPE will prevail.

CONDUCTING RESEARCH AND PRESENTING AN ABSTRACT AS A SECOND-YEAR MEDICAL STUDENT

Recently, I was part of a 6-week-long research internship at the end of which I generated an abstract that I presented at the Annual Neuro-oncology symposium at the Aga Khan University, Karachi. Being a second-year medical student, no one expects you to conduct research on your own, let alone present it at an international conference. Besides that, a second-year medical student neither has the motivation nor the expertise to do that. I did not want to fall prey to this culture. Rather, I took the initiative and wanted to achieve great things early in my career, thus inspiring fellow medical students in the process. Fortunately, the recently established Student Research Committee at Khyber Medical College provided me with an excellent ground, to begin with.

The 3rd Annual Neuro-oncology symposium held at the Aga Khan University, which is one of the prestigious medical schools in Pakistan, was a 3-day event that included keynote lectures, case presentations in front of a tumor board, and paper presentations. Renowned physicians and surgeons from all over the world spoke regarding different topics concerning brain and spinal tumors and presented the advances they made in making cancer therapy better. To sit among such medical professionals and academicians, was humbling and one of the best academic experiences of my life.

My research was a gene study that I contributed for Medulloblastoma under the supervision of Dr. Faisal F. Khan. I was able to recognize the differentially expressed genes in the molecular subtypes of Medulloblastoma and generated a list of FDA-approved drugs that could target them and hence stop tumorigenesis and enhance apoptosis of the tumor cells. This research helped me grab the first spot in the paper presentation session of the symposium. Besides that, experts provided their valuable input on the next steps I could take to arrive at something that might help us get a step closer.

Interacting and learning from professionals currently at the peak of their careers, presenting my research and advocating for it, and winning, boosted my motivation to work even harder. Being among these great professionals has inculcated in me the rigor needed to be one of them and serve humanity. My advice to my fellow medical students would be to set their priorities and start early. As the saying goes “It’s never too late or too early. The time is always just right”.

ADDRESS OF CORRESPONDENCE
Muhammad Awais Khan
2nd-year MBBS student
Khyber Medical College, Peshawar - Pakistan
awais0906.khan@gmail.com
+92-334-1755005