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Editorial

Vitamin B12 – Need of the Body

Mohsin Masud Jan

Editor

What is Vitamin B12?

Vitamin B12 is a water-soluble vitamin that contains the mineral cobalt, so is sometimes called cobalamin. It is naturally found in some foods like tuna, beef and dairy, is added to fortified foods like breakfast cereals, and is available as a dietary supplement or prescription. B12 is a necessary nutrient for the development of the brain and nerve cells, red blood cells and DNA synthesis. Since it is not primarily found in plant foods (though some, like seaweed and mushrooms, can contain small amounts), it is essential for people who follow a vegan and vegetarian diet to supplement or consume foods fortified with B12. Methylcobalamin and 5-deoxyadenosylcobalamin are the metabolically active forms of vitamin B12. However, two others forms, hydroxycobalamin and cyanocobalamin, become biologically active after they are converted to methylcobalamin or 5-deoxyadenosylcobalamin¹⁻².

Vitamin B12 Deficiency

Causes of vitamin B12 deficiency include difficulty absorbing vitamin B12 from food, lack of intrinsic factor (e.g., because of pernicious anemia), surgery in the gastrointestinal tract, prolonged use of certain medications (e.g., metformin or proton pump inhibitors, discussed in more detail below in the section on interactions with medications), and dietary deficiency³⁻⁴. Because people who have difficulty in absorbing vitamin B12 from food absorb free vitamin B12 normally, their vitamin B12 deficiency tends to be less severe than that of individuals with pernicious anemia, who cannot absorb either food-bound or free vitamin B12. Certain congenital conditions, such as hereditary intrinsic factor defects and congenital vitamin B12 malabsorption (Imerslund-Gräsbeck disease), can also cause severe vitamin B12 deficiency³. The effects of vitamin B12 deficiency can include the hallmark megaloblastic anemia (characterized by large, abnormally nucleated red blood cells) as well as low counts of white and red blood cells, platelets, or a combination; glossitis of the tongue; fatigue; palpitations; pale skin; dementia; weight loss; and infertility^{3,4}. Neurological changes, such as numbness and tingling in the hands and feet, can also occur. These neurological symptoms can occur without anemia, so early diagnosis and intervention is important to avoid irreversible damage⁵. In addition, some studies have found associations between vitamin B12 deficiency or low vitamin B12 intakes and depression⁶⁻⁷. In pregnant and breastfeeding women, vitamin B12 deficiency might cause neural tube defects, developmental delays, failure to thrive, and anemia in offspring.

Because the body stores about 1 to 5 mg vitamin B12 (or about 1,000 to 2,000 times as much as the amount

typically consumed in a day), the symptoms of vitamin B12 deficiency can take several years to appear.

Vitamin B12 deficiency with the classic hematologic and neurologic signs and symptoms is uncommon. However, low or marginal vitamin B12 status (200–300 pg/mL [148–221 pmol/L]) without these symptoms is much more common, at up to 40% in Western populations, especially in those with low intakes of vitamin B12-rich foods. The prevalence of vitamin B12 deficiency varies by cutoff level and biomarker used.

Typically, vitamin B12 deficiency is treated with vitamin B12 injections because this method bypasses any barriers to absorption. However, high doses of oral vitamin B12 might also be effective. A 2018 Cochrane Review included three randomized controlled trials (RCTs) that compared very high doses (1,000–2,000 mcg) of oral with intramuscular vitamin B12 for vitamin B12 deficiency in a total of 153 participants. The evidence from these studies, although of low quality, showed that the ability of high oral doses of vitamin B12 supplements to normalize serum vitamin B12 was similar to that of intramuscular vitamin B12.

However, because most people do consume enough through food and the body stores a significant amount of vitamin B12 in the liver, symptoms of B12 deficiency can sometimes take years to appear. The infants of Vegetarians women also have B12 deficiency. The deficiency involves in different disease persons like different types of cancer, cardiovascular disease, stroke, dementia and diabetes also have shown the deficiency of Vitamin B12.

Health Benefits of Vitamin B12

Research has shown that vitamin B12 plays several essential roles in our health. Some benefits include the following.

Red Blood Cell Production

Sufficient vitamin B12 is necessary for producing healthy red blood cells and preventing megaloblastic anemia, a type of anemia that causes large, underdeveloped cells. Symptoms of megaloblastic anemia can include fatigue, pale skin, heart palpitations, loss of appetite, weight loss or infertility.

Brain and Nervous System Health

B12 is required for neurological function and maintaining healthy nerve cells.⁸ Therefore, B12 deficiency can interfere with maintaining healthy function of the nervous system and could even lead to permanent nerve damage over time.

Development for Infants

As an infant's brain develops rapidly, adequate B12 is needed to support healthy brain development and produce red blood cells.⁹ B12 is readily found in breast milk and is fortified into formulas, so infants' needs can

be easily met from consuming these foods regularly. While rare, B12 deficiency can cause failure to thrive and delays in developmental milestones for infants. If left untreated, vitamin B12 deficiency could lead to permanent brain damage over time. If you have concerns about your child, be sure to talk to your doctor and health care team.

Healthy Energy Metabolism

Vitamin B12 plays an important role in energy metabolism. For this reason, if you have a vitamin B12 deficiency, you may feel tired or weak. The good news is that B12 deficiency is generally easy to treat, through increasing food sources, taking a supplement or, in cases of malabsorption, via high-dose injection or nasal spray. Oftentimes, treatments can work very quickly, within 48 to 72 hours. Talk to your doctor to identify an individualized plan for you.

While scientists are studying the effects of B12 supplementation on cancer, heart disease, stroke, dementia or adjunct therapy for viral infections, more evidence is needed to clarify its influence on long-term health.¹⁰

Food Sources of Vitamin B12

Since vitamin B12 is bound to protein, B12-rich food sources include: fish, meat, poultry, eggs, dairy, clams, oysters, beef liver, Fortified breakfast cereals, nutritional yeast and plant-based milk alternatives. If you want to start adding more vitamin B12 food sources to your diet, find food sources that you actually enjoy. You are much more likely to continue eating them if they're foods that can easily be added to your daily diet.

If you follow a vegan diet, use fortified nutritional yeast as well as fortified foods to supplement your diet. You can sprinkle it over pasta, pizza and salads for a cheesy flavor, or mix it into soups or stews. When a product is fortified with B12, a percent Daily Value will be listed on the food label in the vitamins and minerals section. Naturally occurring B12 is not listed on the food label.

Who Could Benefit from Vitamin B12 Supplementation?

While most people get enough from food sources in their diets, people with vitamin B12 deficiency or the following circumstances should consider taking a supplement:

Those following a vegan or vegetarian diet: Since B12 is only naturally found in animal foods, studies have shown that those following vegetarian and vegan diets tend to have low B12 stores. This is especially important for those who are pregnant, since it is necessary for proper fetal brain and nerve system development.

Those with a lack of intrinsic factor: Pernicious anemia is an autoimmune disease that impairs the gut's ability to produce intrinsic factor, which is a protein that is necessary for the absorption of B12.

Those with low stomach acid or medications that decrease stomach acid: Lack of sufficient stomach

acid is the most common cause of B12 deficiency, especially for older adults. And vitamin B12 deficiency affects between 3% and 43% of older adults. Certain medications that reduce or suppress stomach acid taken regularly, such as medications and antacids for gastroesophageal reflux disease (GERD) or peptic ulcer disease, can cause difficulty absorbing vitamin B12 from food. However, fortified foods or supplements do not require stomach acid and can be an excellent choice for people who take these medications.

Those who've had intestinal surgery or digestive disorders: Surgery that impacts parts of the stomach or small intestine, or diseases including Crohn's and celiac disease, can cause impaired absorption of B12. Talk to your doctor about the best care plan for you.

Those using other medications that interfere with absorption: Metformin, a commonly prescribed drug for prediabetes and diabetes, can block absorption of B12 and is strongly associated with B12 deficiency.

Recommended Intakes

Intake recommendations for vitamin B12 and other nutrients are provided in the Dietary Reference Intakes (DRIs) developed by the Food and Nutrition Board (FNB) at the National Academies of Sciences, Engineering, and Medicine. DRI is the general term for a set of reference values used for planning and assessing nutrient intakes of healthy people. These values, which vary by age and sex, include the following:

- **Recommended Dietary Allowance (RDA):** Average daily level of intake sufficient to meet the nutrient requirements of nearly all (97%–98%) healthy individuals; often used to plan nutritionally adequate diets for individuals
- **Adequate Intake (AI):** Intake at this level is assumed to ensure nutritional adequacy; established when evidence is insufficient to develop an RDA
- **Estimated Average Requirement (EAR):** Average daily level of intake estimated to meet the requirements of 50% of healthy individuals; usually used to assess the nutrient intakes of groups of people and to plan nutritionally adequate diets for them; can also be used to assess the nutrient intakes of individuals
- **Tolerable Upper Intake Level (UL):** Maximum daily intake unlikely to cause adverse health effects

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WhatsApp Academy of Ophthalmology: Eye Specialists' Lens: Real-Time Case Discussions and Professional Development. Two-Year Cohort Experience

Aurangzeb Shaikh¹, Ayesha Zeb², Ali Zeb³, Anjali Zeb³, Raj Kumar¹ and Ummay Kulsoom¹

ABSTRACT

Objective: Assessing the efficacy of WhatsApp in knowledge dissemination, Understanding the Influence of WhatsApp on Clinical Decision-Making and Evaluating Long-term Professional Development Benefits.

Study Design: Cross sectional study

Place and Duration of Study: This study was conducted at the at FRPMC/Air University, Karachi from August 2021 to August 2023.

Methods: A cohort of eye specialists, including trainees, ophthalmologists, and academic faculty, participated in a structured program of real-time case discussions facilitated through a WhatsApp group named "WhatsApp Academy of Ophthalmology." Participants were encouraged to share challenging cases, seek input from peers, and engage in multidisciplinary dialog. The discussions encompassed various subspecialties of ophthalmology, including the anterior segment, posterior segment, pediatric ophthalmology, and neuro-ophthalmology.

Results: Over the 2-year period, the "Eye Specialists' Lens WhatsApp group served as a dynamic platform for continuous learning and professional development. Participants reported benefits such as enhanced diagnostic skills, exposure to diverse clinical scenarios, and opportunities for peer learning and mentorship. The real-time nature of the discussions fostered collaboration, accelerated knowledge dissemination, and promoted a culture of lifelong learning among eye specialists.

Conclusion: Real-time case discussions facilitated through platforms such as WhatsApp offer a valuable approach to professional development for eye specialists. The two-year experience with the "Eye Specialists' Lens group highlights the significance of collaborative learning, peer support, and interdisciplinary dialog in advancing clinical practice and enriching the professional lives of ophthalmologists.

Key Words: WhatsApp, Academy, effective teaching tool, assessment, feedback, evaluation.

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INTRODUCTION

An Academic group was created in 2020 with the aim of providing an online academic platform for eye care health professionals. This group consists of 194 national and international members, including postgraduate residents, eye specialists, consultants,

faculty members, and national and international postgraduate fellowship examiners. The WhatsApp Academy of Ophthalmology group is a platform designed for postgraduate trainees, eye specialists, consultants, and academic faculty to connect and share knowledge in the field of ophthalmology. The group aims to promote lifelong learning by sharing clinical research, innovative ideas, and discoveries related to the sense of sight. All members are expected to treat each other with respect and professionalism^{1,2}.

We encourage all members to actively participate by sharing their experiences, insights, and resources related to ophthalmology. This can include case studies, interesting articles, or any developments in the field that could benefit the group. All group members need to follow the set standard rules and regulations as a group member. On average two case discussion per week, anyone can initiate the discussion within the defined rules for authentic references and patients' privacy. The WhatsApp Academy of Ophthalmology represents a groundbreaking approach to professional development

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within the field of ophthalmology. By harnessing the power of WhatsApp, this innovative platform has redefined the landscape of learning and collaboration for healthcare professionals, particularly those specializing in ophthalmic practices. At the core of the WhatsApp Academy of Ophthalmology is the seamless integration of dynamic learning and collaborative initiatives. Through the utilization of WhatsApp, members have been able to engage in vibrant discussions, exchange valuable educational resources, and participate in interactive case studies, all of which serve to deepen their knowledge and expertise in ophthalmology.

Several studies⁵⁻⁹ have explored WhatsApp's potential as an cost-effective platform for knowledge dissemination and collaborative learning. These endeavors not only offer members unique opportunities to engage with leading experts but also serve as immersive learning experiences that contribute to their continuous professional development^{3,4}. One key finding across these studies is the seamless and real-time nature of communication facilitated by WhatsApp, which has been instrumental in promoting active engagement and knowledge exchange among ophthalmic healthcare professionals.

In essence, the WhatsApp Academy of Ophthalmology represents a paradigm shift in the approach to professional development within the field of ophthalmology. Through the innovative use of WhatsApp, this community is driving forward educational innovation, promoting collaborative learning, and ultimately advancing patient care and the broader landscape of ophthalmic practices.

METHODS

An online Google questioner form was created (validation were taken by the senior group members). An online form link was shared with 103 randomly (By randomly selecting group members' cell numbers, one

of the numbers, chosen with a random stop, was included in the study) selected group (including Residents (n=28), eye specialist (n=25), Consultant ophthalmologist (n=26) and faculty members (n=24) with a request to complete the questionnaire. All questions were based on collaboration learning. The methodology adopted for the cohort study encompasses a multifaceted approach to data collection, analysis, and interpretation. Quantitative analysis will be employed to examine metrics such as engagement levels, knowledge acquisition, and frequency of information exchange within the platform

Research Approach: After ethical approval, the study was carried out using cross sectional research design with data collected through a self-administered online survey (quantitative research) on google form. This study was started August 2021 to August 2023 at FRPMC/Air University. An online survey closed ended questionnaire was used to examine the use and impact of WhatsApp Academy of Ophthalmology on group members academic knowledge and team effectiveness.

RESULTS

Out of 103 randomly selected members, 88 members responded (85.43% response rate). Of the 103-study group 28 (28X100/88=31.8%) were postgraduates, 25 (28.4%) eye specialists, 26 (29.5%) consultant eye specialists and 24 (27.3%) were faculty members (Table 1).

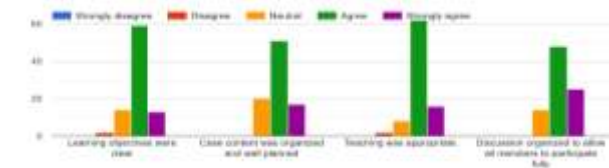
Table No.1: Study Participants

Participants	Total 88 members	out of 100%
Faculty Members	14	15.9%
Consultant	23	26.1%
Eye Specialist	23	26.1%
Post Graduate	28	31.8%

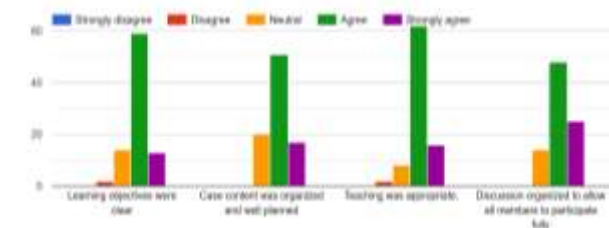
Table 2 Response of study group for effective teaching method

Participants	Group content / case presentation [Case content was organized and well planned]		Group content / case presentation [Teaching was appropriate.]	
Faculty Members	21.4%	Strongly Agree.	21.4%	Strongly Agree.
	64.2%	Agree.	64.2%	Agree.
	14.2%	Neutral.	7.1%	Neutral
	0%	Disagree.	0%	Disagree.
Consultant	13.0%	Strongly Agree.	4.3%	Strongly Agree.
	60.8%	Agree.	82.6%	Agree.
	26.0 %	Neutral.	8.6%	Neutral.
	0%	Disagree.	4.3%	Disagree
Eye Specialist	34.7%	Strongly Agree.	39.1%	Strongly Agree.
	43.4%	Agree.	60.8%	Agree.
	21.7%	Neutral.	0%	Neutral.
	0%	Disagree.	0%	Disagree.
Post Graduate	10.7%	Strongly Agree.	10.7%	Strongly Agree.

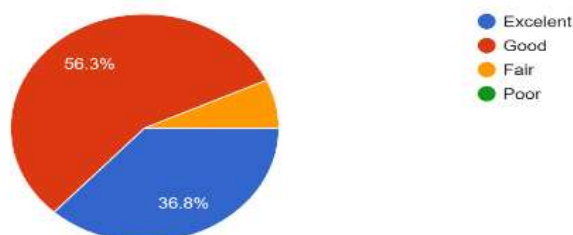
	64.2%	Agree.	71.4%	Agree.
	25%	Neutral.	14.2%	Neutral.
	0%	Disagree.	3.5%	Disagree.



Bar Chart No.1: Group content / case presentation



Bar Chart No.2: Group content / case presentation



Pie Chart No.1: How could you evaluate your entire learning experience as a group member? 87 responses.

The following were the feedback responses for the questions asked in questioner.

Question 1: The primary motive behind joining the WAOO group was identified as follows: 74.4% of respondents indicated learning as their primary reason, followed by 23.3% expressing interest in E-learning experiences, and 2.7% citing time constraints.

Question 2: a. Prior to joining the group, 50% of respondents rated their knowledge level as fair, 35% as satisfactory, 7% as poor, and 13% as very good. b. Following participation in the group, 70% reported a satisfactory improvement in their knowledge, with 15% indicating a very good improvement, 10% reporting fair improvement, and 5% indicating excellent improvement. c. Regarding the group's contribution as a teaching tool to their skills and knowledge, 65% of participants found it satisfactory, 20% rated it as very good, 10% as excellent, and 5% as fair.

Question 3: Group Content/Case Presentation: a. The clarity of learning objectives was acknowledged by 80% of respondents, with 10% strongly agreeing, 8% neutral, and 2% in disagreement. b. Organization and planning of case contents were found agreeable by 70% of respondents, with 12% strongly agreeing, and 13% remaining neutral. c. Regarding teaching

appropriateness, 85% agreed, 10% strongly agreed, 3% were neutral, and 2% disagreed. d. Structured discussions allowing full member participation were endorsed by 68% of members, with 28% strongly agreeing, and 4% remaining neutral.

Question 4: Skill and Responsiveness of the WAOO Instructor:

a. The effectiveness of the instructor as a teacher was acknowledged by 75% of participants, with 20% strongly agreeing, and 5% neutral. b. Clear and organized presentations by the instructor were agreed upon by 80% of respondents, with 15% strongly agreeing, and 5% neutral. c. The instructor's ability to stimulate student interest received agreement from 75% of respondents, with 20% strongly agreeing, and 4% neutral. d. Effective time management by the instructor was acknowledged by 75% of participants, with 10% strongly agreeing, and 15% neutral. e. Availability and helpfulness of the instructor were recognized by 80% of participants, with 15% strongly agreeing, and 4% neutral. f. Prompt grading and useful feedback were acknowledged by 75% of respondents, with 12% strongly agreeing, 10% neutral, and 3% in disagreement.

Question 5: Entire Learning Experience Evaluation: 56.3% of participants rated their learning experience as good, 36.8% as excellent, and 7% as fair.

Question 6: Definition of Group Teaching Activity: 57.4% of respondents considered group activities excellent, 23.8% suggested more teaching activities, 11.95% proposed improvement, and 11.9% found these activities not applicable to the group.

Question 7: Mode of Teaching Effectiveness: Among the research group, 65.5% agreed, and 23% strongly agreed that the WAOO group is an effective teaching method. Overall, 5% strongly disagreed, 4% remained neutral, and 1% disagreed.

Question 8: Recommendation to Colleagues: 98.8% of study participants agreed to recommend the WAOO group to their colleagues as an academic group, while 1.2% disagreed.

DISCUSSION

Study participant demographics and response rate:

The survey revealed valuable insights into the demographics and preferences of the participants. Among the key findings, it was observed that most participants were between the ages of 25 and 35, with an even distribution across gender. In addition, the response rate for the survey was an impressive 87%, indicating a high level of engagement from the participants. These findings provide a solid foundation for analyzing the survey data and drawing meaningful

conclusions about the preferences and opinions of the target demographics.

Reasons for Joining the WAOO Group: Upon analyzing the responses from the survey, it became evident that participants cited various reasons for joining the WAOO group. Furthermore, the survey also highlighted that a significant number of participants were drawn to the WAOO group because of the prospect of gaining access to exclusive industry insights and knowledge-sharing platforms. This aligns with the group's mission to provide valuable resources and foster a collaborative environment for professionals in the field. The survey results truly emphasized the diverse interests and motivations of the participants, highlighting the multifaceted appeal of the WAOO group^{10,11}.

Self-Assessment of Skills Before and After Joining WAOO: Before joining WAOO, a significant percentage of participants rated their confidence in certain skills as moderate. However, after joining the WAOO group, there was a considerable increase in self-assessment ratings, indicating a positive impact on skill development and confidence levels.

This insight not only reflects the value that the WAOO group brings to its members but also underscores the effectiveness of the group's resources and activities in enhancing the professional capabilities of its participants. The data paves the way for further exploration of the specific skill development areas that have experienced the most significant growth and can guide the group in tailoring future offerings to meet the evolving needs of its members^{12,13}.

Feedback on the WAOO's Learning Objectives and Case Presentations (Bar Chart 1): The responses indicated a high level of satisfaction with the learning objectives, with many participants expressing appreciation for the relevance and applicability of the topics covered. Participants also praised the case presentations, highlighting their ability to provide real-world examples and enhance the understanding of complex concepts.

The positive feedback on the learning objectives and case presentations underscores the group's commitment to providing valuable and pertinent content that resonates with its members^{14,15}.

Effectiveness of group discussions in WAOO: Participants stated that the opportunity to engage in meaningful discussions with industry peers allowed them to gain diverse perspectives, exchange valuable insights, and broaden their understanding of various topics. Many also highlighted the interactive nature of the group discussions, emphasizing the collaborative environment that facilitated knowledge sharing and peer learning.

Furthermore, participants appreciated the structured approach of the group discussions, noting that the facilitated conversations effectively addressed relevant

industry challenges and fostered constructive debates around emerging trends and best practices¹⁶.

The overwhelmingly positive feedback on the effectiveness of group discussions underscores the significance of fostering an interactive and knowledge-sharing community within WAOO. It also serves as a testament to the group's ability to create a supportive platform where professionals can actively participate in thought-provoking discussions and collectively contribute to each other's growth and development^{17,18}.

Assessment of the WAOO Group Instructor's Skills and Responsiveness (Bar Chart 2): The feedback highlighted a high level of satisfaction with the instructor's expertise and ability to effectively deliver educational content¹⁹.

Participants commended the instructor for his or her in-depth knowledge of the subject matter, clear communication style, and responsiveness to participant inquiries and feedback. The favorable reviews underscore the crucial role of the instructor in creating a conducive learning environment and imparting valuable knowledge to the WAOO community.

Evaluation of the Overall Learning Experience in WAOO Group (Pie Chart 1): Participants appreciated the structured learning paths offered by WAOO, citing the seamless progression from fundamental concepts to advanced topics as a valuable aspect of their learning journey. Additionally, the availability of resources such as webinars, workshops, and industry-relevant articles contributed to the enriching learning experience and equipped participants with practical insights and knowledge applicable to their professional roles.

Perceptions of Group Teaching Activities: Moving forward, the favorable feedback on the group teaching activities will serve as a cornerstone for the continual development and expansion of peer-led educational initiatives within WAOO, ensuring that members have ample opportunities to both learn from and contribute to the collective knowledge pool.

Effectiveness of WAOO's Teaching Methods: Participants expressed appreciation for the varied teaching techniques utilized, including interactive presentations, case studies, role-playing exercises, and practical demonstrations. These methods were noted to enhance the learning experience by providing different perspectives and catering to diverse learning styles within the group (Table 2).

CONCLUSION

In conclusion, the positive evaluations and feedback gathered from the survey affirm the WAOO group's dedication to fostering a dynamic, inclusive, and impactful learning environment. Joining the WAOO group presents not only the chance to benefit from diverse educational opportunities and innovative teaching methods but also to actively contribute to the collective expertise and growth of the community.

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In Vivo Analysis of Visibility of Maxillary and Mandibular Anterior Six Teeth at Rest

Visibility of
Maxillary and
Mandibular
Anterior Six
Teeth

Sanam Baby, Hina Memon, Naveed Ahmed Memon, Noorulane Mughal, Razia Sultana and Muhammad Rizwan Memon

ABSTRACT

Objective: The Objectives of this study was to determine mean visibility of maxillary and mandibular anterior six teeth among the patients at rest position of lips.

Study Design: Cross-sectional study

Place and Duration of Study: This study was conducted at the at the Prosthodontics department of Liaquat Medical University from March 2022 to December 2022.

Methods: A total of 30 patients with sound maxillary and mandibular anterior teeth free of any restorations, extrinsic stains and caries were included. Measurements were taken with Vernier Caliper. For teeth measurement, internal Jaws of Vernier Caliper were used to avoid lip distortion. Every tooth was measured (mesially, distal, and midway), and the mean was obtained.

Results: The average age of patients were 25.13 ± 3.19 years with 40% male and 60% female. On right side of Arch, mean visibility of maxillary central incisor was 1.77 ± 0.25 mm, lateral incisor 1.24 ± 0.18 mm, and canine 0.41 ± 0.09 mm and mean visibility of mandibular central incisor was 1.49 ± 0.27 mm, lateral incisor 1.50 ± 0.26 mm and canine was 0.85 ± 0.27 mm. Similarly, on left side of Arch mean maxillary central incisor visibility was 1.77 ± 0.25 mm, lateral incisor 1.29 ± 0.21 mm, and canine 0.43 ± 0.06 mm and mean mandibular central incisor visibility was 1.48 ± 0.24 mm, lateral incisor 1.51 ± 0.26 mm and canine was 0.88 ± 0.27 mm respectively.

Conclusion: For treatment planning in esthetic zone we should follow some fundamental guidelines. It is important during replacement or even during restoration of maxillary and mandibular anterior teeth, to consider dento-facial specificities of each person and different natural teeth proportions.

Key Words: Anterior teeth visibility, dento-facial esthetics, anterior teeth measurements.

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INTRODUCTION

Esthetics is one of the primary concern for patients pursuing prosthodontic treatment, as anterior teeth play a significant role in facial appearance¹. Amount of anterior tooth display plays significant role in facial esthetics, as it determines the outcome of removable, fixed as well as of implant prosthodontics treatments^{1,2}. It has been well established that the position of anterior teeth serves as a basis for successful esthetic, functional and phonetics outcomes³.

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The amount of anterior maxillary and mandibular teeth that is visible, is influenced via various factors such as muscle position, age, gender, racial dependency etc. Peoples with smaller lips shows more maxillary incisor surfaces especially central incisors than peoples having longer lips and hence the latter display more mandibular incisors especially central incisors⁴. As compare to females, males generally have longer upper lips, that's why females' maxillary incisors are more visible than males^{5,6}.

Similarly, reduced tonicity of orofacial muscles or reduced upper lips elasticity with increasing tooth support by gingival two-thirds of maxillary incisors leads to less display of maxillary anterior teeth than mandibular teeth^{2,5,7}. If we compare racial differences, more maxillary anterior teeth visibility is evident amongst Blacks than Asians or Caucasians⁶.

In Patients for complete denture treatment and with no previous dental record, dentists rely on subjective assessment, taking aesthetics as a key determine factor for teeth selection which may vary as per experiences of the operator⁸⁻⁹. According to the "law of Harmony" given by Leon William states that, the outline of patient's face is more likely matches with the basic

tooth forms like square, taper and ovoid. Hence, the size and shape of anterior teeth is important for dental as well as facial aesthetics⁶.

One of the common reason for failure of removable and fixed prostheses is dissatisfaction with appearance¹⁰. It has generally been observed that dentists often feel difficulty in selecting size of artificial teeth for the edentulous persons due to lack of experience or exposure to complete denture patients, which suggests that there is a need of continuous training, guidance on artificial teeth selection, their arrangement as well as should have knowledge of visibility of teeth during rest and functional position⁷.

Therefore, the aim of this study was to determine the maxillary and mandibular anterior teeth visibility in dentate persons which will help us in establishing the biometric guides for our local populations as well as, will help us during measurements in teeth selection for fixed, partial or complete prosthesis and therefore provides a comfortable and aesthetically pleasing prosthesis to patients.

METHODS

Using a non-probability consecutive sampling technique, this cross-sectional study was completed in the prosthodontics department at Liaquat Medical University. Patients within 18 to 30 years of age, of both genders, having well aligned anterior maxillary and mandibular teeth which are free of any restorations, extrinsic stains and caries were included for data collection after taking written informed consent from all of these. While patients having Congenital anomalies in anterior teeth, having previous history of Oral and maxillofacial surgery, Orthodontically treated, having Gingivitis and Periodontitis examined clinically and patients with Crowding or spacing specially in anterior teeth assessed clinically were excluded from study.

With the help of Vernier Caliper, measurements of visible portion of tooth for each patient were taken for the designated measured dimensions, to the closest tenth of a millimeter, while patients were seated on dental chair in upright position.

From lowest border of upper lips at resting position up to incisal edges of the incisors and cusp tips in case of canines, visible portion of maxillary anterior six teeth were scaled vertically. The visible surface of the mandibular teeth in the resting position of the lips was measured, starting at the upper border of the lower lip and ending at the cusp tip of the canines and incisal edges in the case of the incisors. Measurements were considered 0 in case of no visibility at the rest. Three measurements (at mesial, distal and midpoint) per tooth were done and the mean finalized. Proforma were filled accordingly. For quantitative variables like age, mean and standard deviation were calculated; for qualitative variables like gender, frequency and percentages were

calculated. Effect modifiers were controlled by stratification. The chi-square test was used, and a P value <0.05 was considered significant.

RESULTS

Thirty patients having maxillary and mandibular anterior teeth free of any restorations, extrinsic stains, and caries were included in this study and their data recorded. Figure one is exhibiting, age distribution of patients. We found average age of the patients in our study 25.13 ± 3.19 years with 40% male and 60% female as revealed in Table-1. Amount of tooth visibility is reported in Table 2. For right side, mean maxillary central incisor was 1.77 ± 0.25 mm, lateral incisor 1.24 ± 0.18 mm, and canine 0.41 ± 0.09 mm and mean mandibular central incisor was 1.49 ± 0.27 mm, lateral incisor 1.50 ± 0.26 mm and canine was 0.85 ± 0.27 mm. Similar for left side mean maxillary central incisor was 1.78 ± 0.25 mm, lateral incisor 1.29 ± 0.21 mm, and canine 0.43 ± 0.06 mm and mean mandibular central incisor was 1.48 ± 0.24 mm, lateral incisor 1.51 ± 0.26 mm and canine was 0.88 ± 0.27 mm. Stratification analysis was performed with respect to gender and age groups, but mean difference was not statistically significant between gender and age groups as shown in table 3 and 4 respectively.

Table No. 1: Age and Gender Distribution of Patients (N=30)

Descriptive statistics for Age distribution

Mean age in years	25.13
Standard Deviation (SD)	+ 3.19

Descriptive statistics for Gender distribution

Percentages

Males	12n (40%)
Female	18n (60%)

Table No. 2: Mean Maxillary and Mandibular Anterior Teeth Visibility Among Patients During Lips Rest Position

Visible Teeth	Right Side of Arch Mean $\pm$ SD	Left Side of Arch Mean $\pm$ SD
Maxillary central incisor	1.77 ± 0.25	1.78 ± 0.25
Maxillary lateral incisor	1.24 ± 0.18	1.29 ± 0.21
Maxillary canine	0.41 ± 0.09	0.43 ± 0.06
Mandible central incisor	1.49 ± 0.27	1.48 ± 0.24
Mandible lateral incisor	1.50 ± 0.26	1.51 ± 0.26
Mandible Canine	0.85 ± 0.27	0.88 ± 0.27

Table No. 3: Mean Visible Portion of Maxillary And Mandibular Anterior Teeth Comparison Between Different Age Groups Among Patients at Rest Position of Lips

Visible Teeth	≤25 yrs n=16		26-30 yrs n=14		P-Value
	Mean	Std. Deviation	Mean	Std. Deviation	
Right Maxilla Central Incisor	1.81	0.25	1.71	0.256	0.298
Right Maxilla Lateral Incisor	1.25	0.20	1.23	0.15	0.832
Right Maxilla Canine	0.42	0.09	0.38	0.08	0.243
Right Mandible Central Incisor	1.52	0.22	1.45	0.31	0.496
Right Mandible Lateral Incisor	1.56	0.22	1.43	0.28	0.188
Right Mandible Canine	0.90	0.27	0.78	0.25	0.224
Left Maxilla Central Incisor Left Side	1.820	0.25	1.72	0.25	0.297
Left Maxilla Lateral Incisor Left Side	1.26	0.19	1.31	0.23	0.513
Left Maxilla Canine	.45	0.08	0.40	0.09	0.186
Left Mandible Central Incisor Left Side	1.52	0.22	1.45	0.31	0.489
Left Mandible Lateral Incisor Left Side	1.56	0.22	1.43	0.28	0.185
Left Mandible Canine Left Side	0.90	0.27	0.85	0.27	0.578

Table No. 4: Comparison of Mean Visibility of Mandibular and Maxillary Anterior Teeth Between Genders During Lips Rest Position

Visible Teeth	Males		Females		P-Value
	Mean	Std. Deviation	Mean	Std. Deviation	
Right Maxilla Central Incisor	1.71	0.26	1.81	0.25	0.312
Right Maxilla Lateral Incisor	1.19	0.16	1.28	0.19	0.203
Right Maxilla Canine	0.39	0.09	0.42	0.09	0.469
Right Mandible Central Incisor	1.47	0.30	1.51	0.25	0.764
Right Mandible Lateral Incisor	1.47	0.29	1.53	0.25	0.539
Right Mandible Canine	0.83	0.33	0.86	0.23	0.786
Left Maxilla Central Incisor	1.72	0.25	1.81	0.26	0.335
Left Maxilla Lateral Incisor	1.18	0.16	1.36	0.22	0.026
Left Maxilla Canine	0.41	0.09	0.44	0.09	0.277
Left Mandible Central Incisor	1.47	0.30	1.51	0.25	0.756
Left Mandible Lateral Incisor	1.47	0.29	1.53	0.25	0.532
Left Mandible Canine	0.85	0.34	0.90	0.22	0.627

DISCUSSION

A smile significantly influences how attractive something seems overall. A beautiful smile typically encourages people to take up prosthetic treatment in particular, as it can boost their self-esteem, advance their professional lives, and live happier lives¹¹. Smile analysis provides information about the relationship between teeth and surrounding soft tissues, which primarily assists in diagnosis and better treatment planning¹²⁻¹⁴.

Understanding several smile criteria, such as smile line and smile arc, is essential to delivering a beautiful smile. Additionally, it's critical to minimize the impact of factors like age and gender on a person's final appearance by being aware of the facts that may influence a smile. A smile line is a single curve that runs from one canine's tip to the other's canine tip¹⁶. A smile line is considered low if half of the maxillary anterior teeth are visible when smiling, average if 1-2

mm of gingiva is visible along with teeth, and high if a significant portion of the gingiva is visible together with teeth¹⁷. On the other hand, the relationship between the incisal edge of the maxillary anterior teeth and the superior border of the lower lip is known as the smile arc¹⁸. A consonant smile arc is parallel relationship between lower lip and anterior teeth, which is esthetically more pleasing¹⁷⁻¹⁸. However, a flat or reversed smile arc is referred to as nonconsonant because it is characterized by a maxillary incisal curve that is either reversed or flatter than the lower lip's curvature. When teeth are worn down, the smile arc typically becomes flat or reversed¹⁹.

Patients in this study had an average age of 25.13 ± 3.19 years. There were 40% male and 60% female. In another such kind of study done by Arigbede and Igwedibia⁴ 59.1% were females and the remaining 40.9% were males, where average range of age of study participants was 17-60 years with mean age of 28.52 ± 9.037 years.

In present study for right side, mean visibility for maxillary central incisor was 1.77 ± 0.25 , lateral incisor 1.24 ± 0.18 , and canine 0.41 ± 0.09 whereas mandible central incisor visibility was 1.49 ± 0.27 , lateral incisor 1.50 ± 0.26 and canine was 0.85 ± 0.27 . Similar for left side mean maxillary central incisor was 1.77 ± 0.25 , lateral incisor 1.29 ± 0.21 , and canine 0.43 ± 0.06 and mean mandibular central incisor was 1.48 ± 0.24 , lateral incisor 1.51 ± 0.26 and canine was 0.88 ± 0.27 . In Alqahtani, et al study²⁰ the mean visibility length for maxillary central and lateral incisor and canine were 9.84, 8.09 mm and 9.08 mm correspondingly. The mean width for the canine remained 7.82 mm, the lateral incisor comprised 6.64 mm, and the central incisor stood 8.74 mm, according to Alqahtani et al²⁰. He observed that the canine/lateral incisor had an apparent width/width ratio of 78.35 mm, while the lateral incisor/central incisor had a mean value of 63.69 mm. The mean values of the apparent width/width ratio of the right and left sides of the arches did not differ in a statistically significant manner²⁰.

Al Wazzan²¹ and Al-Hababbeh⁶ et al. found in their studies, that females are exposing more amount of maxillary central incisors than males. Various studies have documented variations in the manner in which that maxillary incisors display²¹⁻²². According to Awad et al's study²², the maxillary central incisors' mean $\pm$ SD of teeth at rest was 2.40 ± 0.79 mm for females and 2.09 ± 0.92 mm for males. In another study, the measurements for males and females were 1.82 ± 2.80 mm and 4.09 ± 2.27 mm, respectively. However, researcher found that men averaged 1.91 mm and females 3.40 mm. Al-Hababbeh et al's⁶ values, on the other hand, were 2.63 ± 1.15 mm and 3.02 ± 1.96 mm. However, Awad et al²² found in his research that while females display large maxillary lateral incisors, males display much more maxillary canines. Furthermore, contrary to earlier research, a small number of studies found no gender differences in the appearance of the mandibular anterior teeth at rest²³. This inequality in results may be due to racial variances of population of each study, size and types of lips of that area peoples or differences in measurement techniques. Digital video camera²⁴ was used for indirect measurement or direct measurement techniques were performed on the participants with the help of ruler or Bowley gauge in previous studies.

Furthermore, a one survey has also revealed that compared to men, women show more maxillary incisor clinical crowns²⁵. These results are consistent with the current investigation, while some discrepancies would need to be explained by variances in the populations under research and in the methods of measurement.

It has long been thought that prosthodontists evaluate facial aesthetics in connection to the overall harmony of the face. In future days, esthetic concerns considered to be a major factor for patients pursuing prosthodontics

treatments. The arrangement and selection of teeth, particularly the maxillary anterior teeth, are primarily determined by the experience of the clinician. The patient's age, gender, lip size, and desired aesthetic outcome should all be taken into consideration while placing the anterior teeth²¹. Those with shorter upper lips have more of their maxillary teeth visible. Although this appears apparent that, despite the accepted rule, some physicians surprisingly still place anterior teeth 1 to 2 mm below the upper lip border, regardless of lip length. However, one useful technique for determining the appropriate vertical dimension of occlusion is the quantity of anterior teeth that are visible.²⁶⁻²⁷. However, it is equally important to consider the significance of age, gender and lip length while establishing anterior esthetics. Therefore, it is concluded that dependency on only one biometric guideline of incisal show of 2 mm is not sufficient but requires involvement of multiple guidelines collectively.

CONCLUSION

In dentistry esthetics cannot be justified mathematically. We cannot standardize all persons in same way. It is noted that esthetics varies greatly from person-to person. For treatment planning in esthetic zone we should follow some fundamental guidelines. Therefore, it is important during replacement or even during restoration of the maxillary and mandibular anterior teeth, to consider the dento-facial specificities of each person and proportions of various natural teeth.

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The Frequency of Accessory Mental Foramen Using Cone Beam Computed Tomographic Images

Accessory Mental Foramen Using Cone Beam CT Images

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ABSTRACT

Objective: To examine the frequency of AMF using cone beam computed tomography (CBCT) scans.

Study Design: cross-sectional retrospective investigation.

Place and Duration of Study: This study was conducted at the Radiology Department of Khyber College of Dentistry (KCD), Peshawar, Pakistan from 31 January 2024 to April 2024.

Methods: This radio-anatomical research initially evaluated 1000 CBCT radiographs belonging to patients treated over a span of two years. The amount of MF and AMF were recorded. Patients with AMF had their age and sex recorded.

Results: 134 accessory mental foramina belong to males while 25 belong to females aged between 15 and 70 years old, with a mean age of 47.0 years (SD:±17.2). According to the findings of this study, AMF was found in 78 of the 1,000 instances studied. There were 64 cases of unilateral AMF (37 right, 26 left) and 14 bilateral AMF cases (11 with two right and two left, 2 with two right and three left, and 1 with three right and three left). There was only one case when MF was not present.

Conclusion: According to the findings of this study, AMF was found in 78 of the 1,000 instances studied.

Key Words: Cone beam computed tomography; accessory mental foramina; anatomic variation; mental foramen.

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INTRODUCTION

The mental foramen (MF) is an isolated, oval-shaped structure on both sides of the jaw that is located next to the apex of the second premolar⁽¹⁾. The mental foramen is a crucial anatomical characteristic of the buccal region of the jaw⁽²⁾. It permits the inferior alveolar nerve to mature into the mental nerve, providing sensory innervation to the skin, lower lip mucosal membrane, mandibular anterior teeth gingival tissue, and chin skin^(2,3). It has neurovascular bundles, which are mainly composed of tiny arteries and big nerves⁽³⁾. Published research has revealed certain structural peculiarities of the MF, including the existence of auxiliary mental foramina (AMFs)⁽⁴⁻⁶⁾. The nerves and veins that cross the mental foramen must take different routes when AMF is present, and special safety

measures need to be taken while scheduling dental procedures. The supplementary mental foramen is described in several ways in the literature. AMF has been defined by some authors as any foramina that is not the major MF⁽⁷⁾. Conversely, some research indicates that AMFs are simply those foramina that are integrated with the mandibular canal⁽⁸⁾. Conversely, a nutrient foramen is a very small foramen that does not originate in the mandibular canal.⁽⁹⁾

The neurovascular structures that the MF transmits change due to the alteration of AMF, leading to alternative routes. According to Toh et al., the AMF supplied a route for extra mental nerve branches to innervate the skin and mucous membrane, reaching from the corner of the mouth to the median labial area⁽¹⁰⁾. The cadaver investigation by showed that the arteries and nerves passing through the AMF varied in composition and that there was a propensity for an artery to be present in an AMF that was fairly large and distant⁽¹¹⁾. As a result, insufficient knowledge of AMF could explain why local anesthesia levels were insufficient or cause postoperative issues including haemorrhages and neurosensory abnormalities by harming these neurovascular components⁽¹²⁾.

In the case of trigeminal neuralgia, Jha et al. also said that the length of neuralgic pain would increase if an auxiliary mental nerve was not excised during the neurectomy of the mental nerve⁽¹³⁾. Based on these findings, it was essential to identify the AMF before

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any surgical operations including local anesthetic, endodontic and periodontal care, and surgery (including neurectomy, dental implant placement, orthognathic surgery, etc.) could begin in order to achieve beneficial therapeutic outcomes⁽¹⁴⁾.

AMF can be detected using a variety of techniques, including macroscopic examinations of dry skulls, plane radiographs (including periapical, orthopantomogram OPG) and CT scan or cone beam computed tomographic images⁽¹⁵⁾. Cone-beam computed tomography (CBCT)'s ability to provide three-dimensional (3D) pictures that enable thorough analysis of the anatomy of the selected region allows it to overcome the drawbacks of conventional radiography⁽¹⁶⁾. With its comprehensive information on the structures of the maxillofacial complex, CBCT is a priceless instrument that makes it possible to identify and evaluate anatomical differences⁽¹⁷⁾.

To our knowledge till date no studies have been conducted on this topic among the local population. The purpose of this study was to investigate the frequency of AMF using cone beam computed tomography (CBCT) scans.

METHODS

Data Collection Procedure: The Institutional Review Board (IRB) gave its approval for this cross-sectional retrospective study that examined hospital data. The research was done in Peshawar. The radiology department of Khyber College of Dentistry (KCD) provided the CBCT pictures. All patients from KPK, regardless of their socioeconomic status, can access health treatments at Peshawar's Khyber College of Dentistry (KCD), a referral hospital. Each CBCT image was interpreted by the same observer. The CBCT radiographs used in this investigation are currently accessible in the Radiology Department of Khyber College of Dentistry (KCD). CBCT pictures were imported onto the computer using Planmeca Romexis software. A senior radiology technician at KCD took the CBCT radiographs in accordance with strict, standardized scanning procedures and the manufacturer's specifications. A cone beam computed tomography scanner was used to create these radiographs, with an exposure time of 9 seconds and a voxel size of around 400 m, depending on the field of view (FOV). The same examiner assessed each cone

beam computed tomography image to avoid inter-observer differences. They were also evaluated under typical viewing circumstances, which included adjusting the brightness and opacity settings to improve radiograph clarity. The investigator was trained to recognize the mandibular foramen and other landmarks in the mandible using a series of cone beam computed tomographic images prior to performing the radiography examination. The calibration training approach includes practical discussion sessions, demonstrations of how to identify mandibular CBCT landmarks, and instructions on how to utilize the CBCT software to determine the separations between mandibular landmarks.

The study included CBCT pictures of males and females in the age range of 15–70 years, but it excluded CBCT radiographs of patients with pathological lesions in the mandibular mental region and those with bone loss at the MF level in old patients.

The radiographs were recreated and analyzed using at least three planes. The literature defines an AMF as any smaller foramen that emerges from a mandibular canal branch and is situated in close proximity to the MF⁽¹⁸⁾. The presence of the MF and any AMF was assessed for every case. The age and sex of AMF patients were noted.

Statistical analysis: The statistical analysis was conducted using IBM SPSS Version 20.

In order to determine the frequency of one or more AMF, frequency analysis was done.

To search for any possible differences between the gender of the patients and the existence of AMF, the chi-square test was employed.

The level of statistical significance was set at 95%.

RESULTS

AMF was found in 78 (7.8%) of the 1,000 CBCT's studied. There were 64 (6.4%) cases of unilateral AMF (37 right, 26 left) and 14 (1.4%) cases of bilateral AMF (11 cases with two right and two left, 2 cases with two right and three left, and 1 case with three right and three left). There was only one case when MF was not present (Table 1).

The AMF sample included 25 females and 53 males. There was no discernible gender difference. The patients with AMF had an average age of 47.0 years (SD: 17.2 years, range: 15-70 years).

Table No. 1: Distribution of gender of patient with AMF

		Distribution of gender of patient with AMF							
		Total							
		Mental Foramen Absent	2R	2 Lt	3R	3 LT	2R, 2Lt	2Rt, 3Lt	3R, 3Lt
Gender	Male	1	26	13	2	1	7	2	1
	female	0	8	12	1	0	4	0	0
Total		1	34	25	3	1	11	2	1
									78

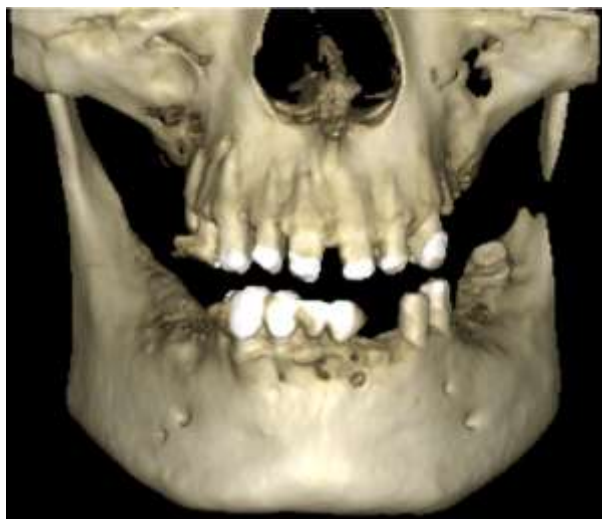


Figure No. 1: Bilateral Accessory mental foramen seen in a CBCT picture that has been surface rendered.



Figure No. 2: CBCT image of patient with Unilateral Accessory mental Foramen on left side of the mandible.

DISCUSSION

AMF is an uncommon mutation linked to mental foramen. It carries a branch of the inferior alveolar nerve that nourishes the same area with the mental nerve and emerges the mandibular canal from a separate foramen. Certain neurovascular problems during procedures like implant implantation and periapical surgery will occur if they go unnoticed. Therefore, the treatment plan is influenced by knowledge about this anatomic variance⁽¹⁰⁾. Planned surgery in the mental region also requires knowledge of the anatomical variances of the MF. It has been proposed that postoperative complications like paralysis or bleeding after implant insertion or dentoalveolar

surgical procedures in this area are caused by a failure to recognize and account for the presence of AMF⁽³⁾. Labio-mandibular paresthesia after endodontic overfilling and surgery has also been connected to it. It is also crucial to be aware of the possibility of multiple mental foramina because an AMF can present as a periapical radiolucency on conventional plain film radiography, potentially misdiagnosing the condition⁽¹⁹⁾.

In this study, AMF was detected in 78 out of the 1,000 CBCT scans, indicating a frequency of 7.8%. This frequency aligns with previous research findings that have reported varying frequencies of AMF in different populations, ranging from 1% to 14%^(20,21). The relatively high frequency of AMF observed in this study underscores the importance of considering this anatomical variation in clinical practice.

According to the findings of present study the unilateral presence of AMF was noted in 6.4% of cases, with a slight predilection for the right side (37 cases) compared to the left side (26 cases).

A study by Lam, et.al.2019 found that the most common anatomical difference among the group of people with AMF was unilateral AMF, occurring 7.8% of the time in the whole population⁽³⁾. According to other research, the range was 2.2-2.2%^(22,23). As was noted in earlier investigations, there was no discernible variation in the frequency of incidence of AMF between sides⁽²⁴⁾.

In the present study Bilateral AMF was observed in 1.4% of cases, with varying patterns of distribution, including cases with two right AMFs, two left AMFs, and combinations of both. According to a study conducted by Lam, et.al.2019 bilateral AMF was found to be 0.3%⁽³⁾, while other earlier research demonstrates a range of 0.5% to 7.9% as documented in the literature⁽²⁵⁾.

It is noteworthy that the absence of the mental foramen (MF) was rare, occurring in only one case. Knowledge of such variations is crucial to avoid complications and ensure the safety and success of procedures in the mandibular region⁽²⁶⁾.

The gender distribution of AMF did not reveal significant differences, with 53 cases in males and 25 cases in females. This lack of gender predilection for AMF is consistent with previous studies^(21,22). It is imperative to recognize, nonetheless, that the study's sample size may have limited the capacity to identify minute gender-related differences in the frequency of AMF. To investigate any possible gender-related variations, greater study with bigger and more varied populations is necessary.

The age distribution of the AMF patients in this study showed an average age of 47.0 years, with a range of 15 to 70 years. It's interesting to note that the age group of 15–25 years old had the highest prevalence of AMF, followed by the age group of 26–40 years old. This

finding suggests that AMF may not be associated with a specific age group but can be encountered in individuals across various age ranges. This observation challenges previous assumptions that AMF may be more common in older individuals⁽²²⁾.

Furthermore, dental implant placement in the mandibular region must take into account the presence and location of AMF to avoid damage to neurovascular structures. Careful assessment through CBCT imaging can aid in treatment planning and minimize the risk of complications associated with implant placement in the vicinity of AMF⁽¹⁸⁾.

CONCLUSION

With a frequency of 7.8%, understanding and identifying AMF is crucial for optimal clinical practice in oral and maxillofacial surgery.

According to the study's findings, gender does not influence the frequency of AMF, indicating its occurrence irrespective of gender.

The study's findings also suggest that AMF occurrence isn't specific to any particular age group.

Author's Contribution:

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Comparative Effect of Maitland Glenohumeral Mobilization and Muligan Glenohumeral Mobilization in Combination With Scapular Mobilization in Patients with Frozen Shoulder

Adeera Azam¹, Esha Dilawar², Ammarah Ikram², Aabroo Zafar², Nowal Nasir² and Nazia Sarfraz¹

ABSTRACT

Objective: The current study is aimed to investigate the comparison of the effect of Maitland glenohumeral mobilization and Mulligan glenohumeral mobilization in combination with scapular mobilization in frozen shoulder patients.

Study Design: Randomized clinical trial study

Place and Duration of Study: This study was conducted at the University of Faisalabad from Feb 2023-Jun 2023.

Methods: The study is conducted on idiopathic or primary adhesive capsulitis, aged between 35 to 55 years on 39 female patients. A convenient sampling technique is used. This is a randomized clinical trial. Randomization is performed by lottery method. Patients are divided into two groups, Group A received Mulligan technique with scapular mobilization and Group B received Maitland Technique with scapular mobilization.

Results: The pain and disability score analysis shows significant statistical results in Group A subjects in comparison to Group B. The mean of abduction range, external rotation, internal rotation, and flexion showed significant results ($p < 0.05$) in Group A as compared to (Maitland group) group B. The mean score of SPADI reduced to 31.6842 ± 6.89648 in Group A (Mulligan mobilization with scapular mobilization), whereas in Group B (Maitland mobilization with scapular mobilization) the mean has improved to 39.6500 ± 2.23077 . The range of motion score analysis for intergroup comparison showed the strength significantly improved in Group A subjects in comparison to Group B subjects.

Conclusion: Results of this study demonstrate that the Mulligan method with scapular mobilization is an effective treatment approach compared to the Maitland method with scapular mobilization in managing a frozen shoulder.

Key Words: Frozen shoulder, Mulligan mobilization, Maitland mobilization, scapular mobilization, Shoulder joint.

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INTRODUCTION

Frozen shoulder (FS) is defined as a painful and limited musculoskeletal disease with passive and active range of glenohumeral joint movement limitation, mostly external rotation and abduction of shoulder joint removal⁽¹⁾.

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Frozen shoulder is a musculoskeletal disorder where the capsule of the connective tissue becomes steep and stiff, inflamed and shortened.

Frozen shoulder is a prevalent shoulder disorder that is treated by a variety of medical professionals including orthopedic surgeons, rheumatologists, and physiatrists. However, it is also one of the most misunderstood conditions of the shoulder. A 1966-2008 National Library of Medicine Citations Medline search indicates 3,586 references when using the search term frozen shoulder. Codman was the first who introduced and used the term, "Frozen shoulder." It is one of the few conditions that affect the connective tissue forming the capsule of the glenohumeral joint of the shoulder⁽²⁾.

Usually self-limiting, adhesive capsulitis. Many recent investigations have shown that adhesive capsulitis can cause long-term function and disability⁽²⁾. Shoulder discomfort and stiffness early on are unusual symptoms. Movement, especially abduction and

external or internal rotation, causes scapulohumeral joint discomfort⁽³⁾.

Moving the scapula and humerus interrupts rhythm. Diseases can disturb scapulohumeral rhythm and produce dysfunction⁽⁴⁾.

Physiotherapy is used in most frozen shoulder treatments. Exercise, massage, electrotherapy, and manual therapy are common therapies. Clinical shoulder mobilisation uses Kaltenborn, Maitland, and Mulligan manual therapy⁽¹⁾ Angular and translational mobilisations increase ROM. After introducing Maitland, the International Maitland Teachers Association developed manipulation techniques for neuromuscular analysis and treatment⁽⁴⁾.

Mulligan Mobilization with Motion (MWM) is a set of manual therapy techniques that are use in musculoskeletal pain treatment. It involves manually applying a sustained glide to the joint by a therapist while actively performing a concurrent joint movement by the patient⁽⁵⁾.

Because the scapulo-thoracic (ST) joint is made up of muscles, not similar to synovial joints, inferior shoulder tightness in Adhesive capsulitis may affect shoulder flexion and abduction. Scapular mobilization (SM) can release tightened muscles by breaking the adhesions, which may result in improved scapular movement. Improved shoulder movement may also be associated with increased scapular movements.

The current study aimed to provide a proper treatment plan starting from baseline treatment to selected treatment techniques. It also provided recommendations for other therapists to use these combinations of techniques rather than one technique and provide beneficial effects for patients.

METHODS

A randomized clinical trial was performed using a non-probability convenient sampling technique. The total sample of this study was 40, randomly divided into two groups, 20 patients in each group. One patient was dropped out after 6 sessions. So, the sample size was confined to 39 with the help of the following formula

$$n = 2SD^2(Z_{\alpha/2} + Z_{\beta})^2 / d^2$$

*S.D= Standard Deviation, d= effect size= difference between the mean values,

$$Z_{\alpha/2} = Z$$

$0.05/2 = 1.96$ (from Z table), $Z_{\beta} = Z_{0.20} = 0.842$ (from Z table) at 80% power.

Patient data collected from Nusrat Abdul Rauf Centre for Enablement and Prime Care Hospital. After research approval committee overview approval, this study was finished four months later. Participants were 35–55-year-old women with limited passive range of motion (PROM) with a 50% reduction in shoulder movements (flexion, external rotation, internal rotation, and abduction), shoulder pain (3-7 on NPRS), pain persisted

for 4-8 months, capsular restriction of ROMs, and frozen shoulder stage II.

Different metrics were used. I assess pain, II disable. Two-way SPADI. A 0-10 pain scale works. 10.5 10-point pain scale questions. It hurts 50. 8 disability 10-point questions. Questions 0-10 discussed difficult everyday duties. Zero means “no difficulty” and 10 meant “so difficult it requires help”. Each incorrect answer lowers SPADI's 130 score by 10. Patients can get 72 function points. Ultimate function score = $72/130 = 0.55 \times 100 = 55$. We assessed pre-treatment, 6th, and 12th session universal goniometer shoulder ER, ABD, and IR.

Both groups received physical therapy for 4 weeks with 6 sessions/ week⁽¹⁰⁾.

Group A received 5 minutes of ultrasound before exercise and 15 minutes of burst TENS after exercise⁽⁶⁾. Exercise stretching 2 sets of 3 reps, 10 sec stretch. Mulligan glenohumeral mobilisation: postero-lateral, inferior glide, lateral distraction. 3 x 5 reps. Rotations, superior and inferior gliding, and scapular distraction. Two sets of three repetitions with 10-second rests. Group B received 5 minutes of ultrasonography before exercise and 15 minutes of burst TENS after exercise. Two 3-rep sets of 10-second stretches. Maitland posterior, anterior, and inferior glide glenohumeral mobilisation. (3) sets (3) repetitions (10). Rotations, superior and inferior gliding, and scapular distraction. Two sets of three repetitions with 10-second rests⁽⁶⁾.

Patients were randomly allocated into one of these two intervention groups: Mulligan and Maitland group. In a total treatment period of four weeks, each group contained 20 patients who received shoulder mobilization three times a week. In addition, patients in the two groups received scapular mobilization and shoulder stretching exercises. Data was analyzed using windows software SPSS version 22.0. independent sample t-test was applied to measure difference between two groups. The significance level was set to 0.05.

RESULTS

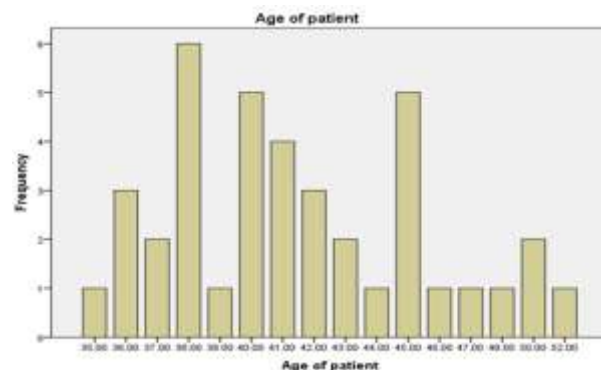


Figure No. 1: Demographics of age depicted

Forty participants were assessed for eligibility. one subject was dropped out from group A after completion of 6 sessions due to health issues.

Between Group Analysis Independent sample t-tests were applied to analyze the significance between variables of both the treatment and control group.

Table No. 1: Mean Pain– Independent sample group statistics

	Groups of treatment	N	M	SD	P
NPRS baseline	Mulligan Mobilization with Scapular Mobilization	19	6.3684	.76089	.114
	Maitland Mobilization with Scapular Mobilization	20	6.7000	.47016	
NPRS after the 6th session	Mulligan Mobilization with Scapular Mobilization	19	4.4211	.60698	.031
	Maitland Mobilization with Scapular Mobilization	20	4.9000	.71818	
NPRS after the 12th session	Mulligan Mobilization with Scapular Mobilization	19	2.2632	.56195	.064
	Maitland Mobilization with Scapular Mobilization	20	2.7500	.96655	

Using the independent samples t-test, both groups' mean shoulder pain values improved. In the independent sample T-test, both treatment groups exhibited significant differences ($P=.114$) in pain measures at baseline. After the 6th session, both groups were statistically significant, and after the 12th session, they were not. Patients' pain levels improved

significantly after the 6th session but not after a baseline or 12th session.

Range of Motion (ROM) Pre-treatment, 6th, and 12th sessions are used to assess range improvement between groups using the Independent T-Test. Significance is determined on $p\text{-value} \leq 0.05$.

Shoulder External Rotation Range

Table No. 2: Mean shoulder ER ROM – Independent sample group statistics

	Groups of treatment	N	M	SD	P
Shoulder external rotation baseline AROM	Mulligan Mobilization with Scapular Mobilization	19	31.3158	2.88776	.731
	Maitland Mobilization with Scapular Mobilization	20	31.6500	3.13344	
Shoulder external rotation AROM after 6th session	Mulligan Mobilization with Scapular Mobilization	19	44.2105	2.89787	.007
	Maitland Mobilization with Scapular Mobilization	20	41.4500	3.17017	
Shoulder external rotation AROM after the 12th session	Mulligan Mobilization with Scapular Mobilization	19	65.1579	3.00487	.000
	Maitland Mobilization with Scapular Mobilization	20	59.8500	4.00362	

Both groups' shoulder ER mean values improved using the independent samples t-test.

An independent sample t-test showed no significant shoulder external ranges pre-treatment differences between Mulligan and Maitland ($P=.731$). At the end of

treatment, the mulligan group had significantly improved shoulder external range of movement ($p=.007$, $p=.000$) after 6 and 12 sessions.

Shoulder Abduction Range

Table No. 3: Mean shoulder ABD ROM – Independent sample group statistics

	Groups of treatment	N	M	SD	P
Shoulder Abduction baseline AROM	Mulligan Mobilization with Scapular Mobilization	19	84.5263	3.45396	.984
	Maitland Mobilization with Scapular Mobilization	20	84.5500	3.69174	
Shoulder abduction AROM after 6th session	Mulligan Mobilization with Scapular Mobilization	19	111.0000	6.63325	.000
	Maitland Mobilization with Scapular Mobilization	20	99.5500	4.72925	

Shoulder abduction AROM after the 12th session	Mulligan Mobilization with Scapular Mobilization	19	141.0526	5.91114	.000
	Maitland Mobilization with Scapular Mobilization	20	131.6000	6.64435	

Independent sample t-test indicated no significant difference ($P=.984$, $P=.079$) in shoulder abduction ranges pre- and post-treatment. The mulligan group improved (.007) after the 12th session.

Because $p>0.05$, independent sample t-test showed no significant difference ($p=.491$, $p=.105$) between groups for shoulder internal ranges pre-treatment and post-6th sessions. The mulligan group exhibited considerable improvement after the 12th session ($p<0.000$).

Table No. 4: Mean shoulder IR ROM – Independent sample group statistic/ Mean SPADI – Independent sample group statistics

Shoulder Internal Rotation Range	Groups of treatment	N	M	SD	P
Shoulder internal rotation baseline AROM	Mulligan Mobilization with Scapular Mobilization	19	30.2632	4.29266	.491
	Maitland Mobilization with Scapular Mobilization	20	29.3500	3.91051	
Shoulder internal rotation AROM after 6th session	Mulligan Mobilization with Scapular Mobilization	19	41.5789	4.79949	.105
	Maitland Mobilization with Scapular Mobilization	20	39.1000	4.50614	
Shoulder internal rotation AROM after the 12th session	Mulligan Mobilization with Scapular Mobilization	19	59.2632	4.70038	.000
	Maitland Mobilization with Scapular Mobilization	20	53.1000	3.59678	
Total SPADI Score	Groups of treatment	N	M	SD	P
SPADI total baseline	Mulligan Mobilization with Scapular Mobilization	19	67.4737	7.19852	.102
	Maitland Mobilization with Scapular Mobilization	20	70.6500	4.38028	
SPADI after 6th session	Mulligan Mobilization with Scapular Mobilization	19	54.7368	8.27206	.042
	Maitland Mobilization with Scapular Mobilization	20	59.0500	3.80408	
SPADI after the 12th session	Mulligan Mobilization with Scapular Mobilization	19	31.6842	6.89648	.000
	Maitland Mobilization with Scapular Mobilization	20	39.6500	2.23077	

After the 12th session of intervention showed significant decline in SPADI score Group A (mulligan group) which showed statistically significant results.

DISCUSSION

The current study includes idiopathic frozen shoulder patients. Stage 2 frozen shoulder patients are 35–55 years old. One study examines primary or idiopathic frozen shoulder. Controlled DM for over 6 months in 30 40–60-year-olds⁽⁷⁾. This study found no significant difference in pain reduction between the Mulligan and Maitland groups after 12 sessions of treatment. Similarly, another study found no significant difference in treatment response (physiotherapy with Maitland mobilization) and control group in shoulder pain patients⁽⁸⁾. Before and after intervention, one study supporting this investigation observed VAS End-range

mobilization and movement group mobilization mean scores were negligible⁽⁹⁾.

The current study showed significant shoulder range of motion improvements in both groups. The shoulder external rotation range improved significantly in Group A (mulligan and scapular mobilization) compared to Group B.

Group B improved flexion, abduction, and external rotation, but not internal rotation or extension, according to one research. Bending, extension, abduction, and external rotation improved significantly in the Mulligan group⁽¹⁰⁾. Comparing anterior and posterior joint mobilizations in frozen shoulder patients to enhance external rotation supported the results of the one research⁽¹¹⁾.

One study found that mulligan and Maitland treatments for adhesive capsulitis provide similar pain alleviation and functional range. Mulligan mobilization and UST

improved all mobility ranges, especially external and internal rotation, better in Group B⁽¹²⁾. In this study, both groups had a substantial decrease in SPADI score, however Group A (mulligan mobilization with scapular mobilization) had a much lower score. The pain threshold and disability subscale score decreased significantly after 1 week of intervention. Mulligan's total SPADI score indicated disability improvement over the control group.

One study measured SPADI and shoulder ROM in all positions individually before and after mobilization therapy. Both before and after treatment, end-range mobilization with scapular mobilization improved ROM and functionality more than individual mobilization. Mulligan mobilization produced statistically significant improvements in this trial, as did both groups, however the Mulligan group improved more than the Maitland group. Compared to stretching, Mulligan's mobilization improved pain, range of motion, physiotherapist and patient satisfaction, and shoulder score. The first study to show that Mulligan's approach outperforms stretching exercises over three months together with immediate therapeutic effects⁽¹³⁾. Scapular mobilization in combination with end-range GH mobilization may be an effective and efficient conservative treatment option to improve the symptoms associated with adhesive capsulitis.

CONCLUSION

Both treatments were concluded to be successful in relieving pain, improving functional status, and increasing ROM in subjects under observation. There was marked improvement in group A (mulligan mobilization with scapular mobilization) related to pain relief. Improvement in ROM as well as SPADI so it is concluded that it is a superior method to deal with frozen shoulder patients as compared to Maitland mobilization.

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Comparing Non-Technical Skills in Neonatal Resuscitation Teams: Performance Across Medical Specialization

Comparing Non-Technical Skills in Neonatal Resuscitation Teams

Hina Khan¹, Muhammad Yousaf Raza² and Romana Altaf³

ABSTRACT

Objective: The initial breath of a newborn is a critical milestone, marking the transition from placental dependence to self-sufficiency. Despite most infants adapting smoothly, some require resuscitation. This audit was conducted to analyze the impact of non-technical skills on neonatal resuscitation team performance across three medical specializations: pediatricians, obstetricians, and anesthesiologists.

Study Design: observational study

Place and Duration of Study: This study was conducted at the Medicare hospital Rawalpindi, between February and March 2024.

Methods: Video recordings from 60 delivery suites at Medicare hospitals were analyzed, assessing non-technical skills using the Global Assessment of Team Performance (GAOTP) checklist. The GAOTP measures six key domains: communication with patients/parents, task/case management, leadership and teamwork, situational awareness, communication between team members, and environment of the room. Each dimension was rated on a Likert scale from 1 to 5.

Results: Pediatricians scored the highest average non-technical skill score of 24.2, followed by anesthesiologists with 20.1, and obstetricians with 17.2, with statistically significant differences ($p < 0.05$). Pediatricians excelled in "environment of the room," "teamwork and leadership," "communication and situational awareness," and "task management," highlighting the importance of effective communication and clear leadership. This study underscores the need for comprehensive training programs that address both technical and non-technical skills to enhance team performance in critical medical situations.

Conclusion: Our study highlight that comprehensive training in both technical and non-technical skills is vital for improving team performance in high-pressure medical situations

Key Words: neonatal resuscitation, non-technical skills, medical specialties, Global assessment of team performance

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INTRODUCTION

The initial breath a newborn takes is a critical milestone, marking the shift from dependence on the placenta to self-sufficiency¹. A failure to successfully transition can pose significant risks, contributing to a considerable proportion around 2.7 million annual neonatal deaths worldwide².

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Efforts to improve neonatal care is a universal need and evidence shows that even in developed countries, care quality sometimes falls short during this crucial period. Healthcare providers in delivery rooms must be skilled in supporting newborns through this transition, as well as in resuscitation. While most infants adapt smoothly to life outside the womb, some require additional interventions. The resuscitation process, often outlined in a step-by-step algorithm, may be rarely used in its entirety. As a result, healthcare teams might struggle to gain the experience needed for a coordinated response. Success in these scenarios depends not just on clinical expertise but also on a set of competencies known as non-technical skills, which encompass situational awareness, leadership, communication, teamwork, managing stress and decision-making³.

Unfortunately, limited evidence available on exact role of these non technical skills in the effectiveness of neonatal resuscitation. Understanding how these skills influence team performance during critical moments is crucial for improving outcomes. A potential method for investigating this aspect involves video recording

resuscitation teams in action². This technique allows for detailed analysis of both technical and non-technical performance, providing insights into teamwork, communication, and other factors that contribute to successful resuscitations^{1,4-6}.

Predicting which newborns will have trouble transitioning and require resuscitation can be challenging. Consequently, the responsibility for initial resuscitative measures often falls on first encountered person like midwives and obstetricians. Given this uncertainty, it is vital to assess the non-technical skills of interdisciplinary teams, including obstetricians, pediatricians and anesthesiologists. This audit aimed to use video recordings in delivery rooms to assess the level of non-technical skills among above mentioned specialized teams, with the goal of identifying areas for improvement and ultimately enhancing neonatal outcomes.

METHODS

This audit was conducted between February and March 2024, factual video recordings were collected from 60 delivery suites at Medicare hospitals to study newborn care during childbirth. Each suite was equipped with two or three high-definition mini-dome surveillance cameras and a ceiling-mounted microphone, providing an angled view of the room, including the neonatal resuscitation table. The recordings were automatically activated via Bluetooth. However, if the pregnant woman is not willing to be the part of this study, no recordings were made. The sixty recorded deliveries were divided into three groups based on the teams responsible for neonatal resuscitation: the anesthesia team, the obstetrician team, and the pediatrician team. Each team was involved in 20 resuscitations, resulting in 20 instances led by anesthesia, 20 by obstetricians, and 20 by pediatricians. All these teams were assessed for their non-technical skills during the neonatal resuscitation.

Inclusion: The inclusion criteria for this study were vaginal birth at gestational age of 34 weeks or more and cases where the newborn showed an insufficient response to stimulation. Each video was 9 minutes in duration, beginning 2 minutes before delivery to capture any preparation, and ending 7 minutes after delivery, regardless of the total video length. This approach ensured consistent observation time and minimized potential bias due to longer videos, which could lead to altered team performance or changing team members.

Exclusion: Women refused to participate and women delivered before 34 weeks of gestation.

To assess the non-technical skills of interdisciplinary teams during these recordings, the Global Assessment of Team Performance (GAOTP) checklist, built by Morgan et al^{7,8}, was used. This tool was chosen among several validated instruments⁹ because it is specifically

designed to assess non-technical performance in delivery rooms. The GAOTP checklist assesses following key domains:

1. Communication with Patients/Parents: Excellent performance involves sharing information with parents (family) and involving them in the newborn's care when appropriate.
2. Task/Case Management: This measures the team's ability to recognize the urgency of the clinical situation, set and communicate goals, and effectively utilize resources.
3. Leadership and Teamwork: Excellent performance is indicated when roles of team members are quickly recognized, a leader is identified, participants are motivated and roles and responsibilities are clear.
4. Situational Awareness: This dimension looks at early appreciation and prompt response to critical situations, timely summoning of extra personnel, and vigilance throughout the clinical event.
5. Communication between Team Members: A focus on clear communication with specific instructions, acknowledgment of messages, and confirmation that requested actions were completed indicates strong performance.
6. Environment of the Room: This dimension assesses whether the environment is orderly and controlled, with calm voices and no visible signs of stress or fatigue among team members.

Each dimension was rated on a Likert scale from 1 to 5, where "1" represents a poor non-technical score, "3" represents an average score, and "5" represents excellent performance. The overall GAOTP score was the mean of the six dimensions. Two physicians, experienced in using the GAOTP, independently rated all the videos, with each reviewer blinded to the other's ratings.¹⁰

RESULTS

Majority of the women, 50%, falls within the 21-25 age range. Most women, 65%, were multigravida. Primary education is the most common level of education, with

Table No. 1: Variables with regard to age, prity and education

Variable		frequency	Percentage
Age	15-20	02	3.3 %
	21-25	30	50 %
	26-30	25	41 %
	31-35	3	10 %
Prity	Primigravida	21	35%
	multigravida	39	65%
Education	Uneducated	14	23.3 %
	Primary	25	41.2 %
	Secondary	21	35%
Area of residence	Urban	45	75%
	Rural	15	25%

Table No. 2: Variables with regard to gestational age

Variable		Frequency	%tage
Gestational age	34-37weeks	22	36%
	>37 weeks	44	73%

41.2% had completed it. A significant majority, 75%, live in urban areas. Most of the women 73% had gestational amenorrhea of more than 37 weeks.

Our study evaluated the non-technical skills of three medical teams responsible for neonatal resuscitation using a Likert scale to assess their performance in a test scenario. These teams comprised pediatricians (Group 1), obstetricians (Group 2), and anesthesiologists (Group 3). The results showed significant differences in non-technical skill levels among the groups, suggesting that the team composition affects the quality of neonatal resuscitation.

The pediatricians in Group 1 achieved the highest average non-technical skill score of 24.2, with a range of 20 to 26 and a standard deviation (SD) of 3.4. The obstetricians in Group 2 had a mean score of 17.2, with a broader range of 15 to 19 and an SD of 7.9. The anesthesiologists in Group 3 achieved an average score of 20.1, with a range of 18 to 22 and an SD of 6.0. The differences in scores between these groups were statistically significant, with a p-value less than 0.05, Figure 1.

Further analysis revealed that the pediatricians (Group 1) demonstrated superior performance in several key areas of non-technical skills. They excelled in "environment of the room," "team work and leadership," "communication and situational awareness," and "task management." The pediatricians' higher scores in these areas contributed to their overall stronger performance, with statistically significant differences compared to both obstetricians and anesthesiologists ($p < 0.04$)

**Figure 1: Comparison of Non-technical skill between different teams**

DISCUSSION

Effective communication emerged as a crucial element for teamwork in critical situations. A competent leader

is key, providing guidance on patient care and recognizing essential tasks. The leader's role involves monitoring the situation, being vigilant for what might be needed next, and regularly assessing the clinical progress.

The pediatricians (Group 1) in the study showed exceptional performance in non-technical skills, particularly in "room environment," "teamwork and leadership," "communication and situational awareness," and "task management." These results underscore the importance of a clear leader who can coordinate the team effectively.

Training physicians in both technical and non-technical skills presents a significant challenge, especially for younger practitioners. While developing technical skills is crucial, it's equally important to cultivate competencies in communication, teamwork, and leadership. The ability to manage tasks effectively and maintain situational awareness is crucial for optimal patient outcomes. This study highlights the need for comprehensive training programs that address both technical and non-technical aspects of medical practice. Studies on non-technical skills—including leadership, situational awareness, communication, teamwork, decision-making, and stress and fatigue management—have revealed that the importance of these skills varies based on context, specific tasks, and medical specializations. For example, the demands on resuscitation teams that assemble ad hoc for emergency situations are quite different from those on surgical teams carrying out carefully planned procedures.

In a resuscitation scenario, teams require heightened situational awareness and rapid decision-making due to the high-pressure and unpredictable nature of the task. Communication and teamwork become even more critical when every second counts. In contrast, surgical teams in a controlled environment may focus more on leadership and task management, given the pre-planned nature of their work.

Our study has few limitations. The study had only nine recorded cases, with each team observed in only three resuscitations. This limited sample size can lead to reduced statistical power and affect the generalizability of the findings. The study was conducted in a single hospital network (Medicare), which could limit the generalizability of the results to other hospitals with different protocols, team structures, or patient demographics. While the study evaluated non-technical skills, it does not correlate these skills with actual neonatal outcomes.

CONCLUSION

Our study highlight that comprehensive training in both technical and non-technical skills is vital for improving team performance in high-pressure medical situations.

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Effectiveness of Posterior Laminoforaminotomy in the Management of Lateral Cervical Soft Disc Herniation

Laminoforaminotomy
in the Management of
Lateral Cervical Soft
Disc Herniation

Mohammad Nasir and Fayyaz Ahmad

ABSTRACT

Objective: The outcome of this study will therefore determine the suitability of posterior laminoforaminotomy in the treatment of lateral cervical soft disc herniation.

Study Design: observational study

Place and Duration of Study: This study was conducted at the Department of Neurosurgery MTI HMC Peshawar from July 2022 to June 2023.

Methods: A total of fifty four patients were included in this study for the surgical management of lateral cervical soft disc herniation with laminoforaminotomy. The measure of effectiveness was done using Odom's criteria. All the analysis of the data was done employing SPSS.

Results: The patients' mean age was 42.04 ± 11 , 57 years. The Odom's criteria to determine the efficacy were excellent in 39 (72.2%) patients, good 10 (18.5%), fair 3 (5.6%) and poor 2 (3.7%).

Conclusion: Posterior laminoforaminotomy can be recommended as an effective method of surgical treatment for lateral cervical soft disc herniation.

Key Words: Soft disc; Spine surgery; cervical foraminotomy; spondylosis

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INTRODUCTION

Cervical spine soft disc herniation is defined as the bulging of intervertebral disc beyond its normal margins and compressing the adjacent neural tissue^{1,2}. Lateral herniation is the extrusion of disc material into the outside of the spinal canal and could possibly impinge on nerve roots as they exit the neural foramen³. This condition often manifests as radiculopathy, a condition characterised by pain, numbness and muscle weakness in the area served by the affected nerve. At times, conventional treatments such as conservations and physical therapies can help alleviate the problems. However, if the symptoms persist or worsen, then the surgical surgery may be needed⁴⁻⁶.

Lateral cervical soft disc herniation is a major clinical challenge in the sphere of spinal disorders; it often causes severe pain and neurological deficits⁷. What is more, the posterior laminoforaminotomy (PLF) is now one of the most significant surgical ways of treatment for this specific disease.

This is an operation that is less invasive and which is carried out on the posterior cervical region. It focuses on the neural foramen which is a critical region where nerve root entrapment occurs due to herniated disc fragments^{8,9}.

PLF is derived from the principles of decompression with the aim of alleviating the neural compression and return the nerve roots to their normal state of functioning of the affected nerves¹⁰. Unlike the conventional open operations, PLF is characterized by minimal access and requires small incisions and special instruments to get to the intended area through the back part of the spine¹¹. Therefore, the effectiveness of posterior laminoforaminotomy depends on the ability of giving a direct and selective approach to the neural foramen to give the surgeon a view of the herniated disc and treat it correspondingly. This is because accessing the procedure through the back side minimizes the handling of the spinal cord; hence the possibility of experiencing challenges associated with the more invasive methods^{12,13}.

The rationale for posterior laminoforaminotomy in the treatment of lateral cervical soft disc herniation is that it is a selective procedure that is less traumatic and capable of providing adequate decompression of neural elements. Due to the constant advancements in both technology and process, this surgical method can be a more useful option in assisting patients who wish to have the troublesome symptoms of lateral cervical disc herniation relieved. Further clarification of the specificities and outcomes associated with this still-evolving component of spinal surgery will be obtained

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from the further analysis of clinical studies and cases. The objective of the study is to evaluate the role of posterior laminoforaminotomy in treating patients with lateral cervical soft disc herniation.

METHODS

This observational study was carried out in the MTI HMC Neurosurgery department, Peshawar from the months of July 2022 to June 2023. Posterior cervical laminoforaminotomy was performed in fifty four patients for the management of lateral cervical soft disc herniation and this did not exclude any patient based on the age or gender. This investigation also did not include patients who had a prior cervical anterior or posterior fusion or those who had undergone laminectomy or multi-segment, or bilateral posterior cervical fusion at the same time.

Patients or their families were offered informed consent after the research proposal was approved by the hospital's ethics council. The reviewed patients' records included their age, gender, handedness, previous conditions, current diagnosis, neuroimaging findings, treatment details, and outcomes with focus on the symptoms that improved or worsened and their aftermaths. Cervical radiculopathy was confirmed using magnetic resonance imaging for diagnosis while computed tomography was used to establish the cause of the cervical radiculopathy such as foraminal stenosis, osteophyte or lateral disc herniation. X-rays were used for assessing the straightening of the spine, height of disc, and kyphotic deformity. NCS and EMG were done in some cases where multiple levels were affected to determine which level was involved. Odom's criteria were used to assess the Effectiveness of the procedure. Sample size was determined by openepi, previous proportion of fair outcome 3. 6%, margin of error 5% and confidence interval of 95%. Data entry was done using a form developed from the study tool while the analysis of the patients' data was done using Statistical Package for Social Sciences (SPSS) version 21.

RESULTS

The present study was under taken on 54 patients having mean age of 42.04 ± 11.57 years. The male

patients were 35 of them while the female patients were 19 in number. The symptoms upon presentation was which included pain in the arms 29 (53. 7%), pain in the neck 12 (22. 2%), motor weakness 7 (13%) and tingling with numbness was seen in 6 (11. 1%) patients. The levels of cervical discs involved are indicated in table 2. The outcome based on the Odom's criteria was excellent in 39, good in 10, fair in 3 and poor in 2 patients. Two patients developed infection in the post-procedure period, one underwent reoperation and one patient had CSF leak.

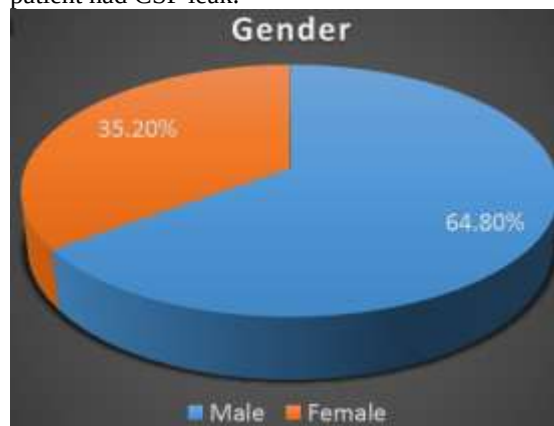


Figure No. 1: Gender distribution

Table No. 1: Cervical discs levels

Cervical discs levels	Frequency	Percent
C3-4	3	5.6
C4-5	4	7.4
C5-6	16	29.6
C6-7	31	57.4
Total	54	100.0

Table No. 2: Efficacy of the treatment

Efficacy of the treatment	Frequency	Percent
Excellent	39	72.2
Good	10	18.5
Fair	3	5.6
Poor	2	3.7
Total	54	100.0

Table 3: Association of the efficacy of the treatment with gender

		Gender		Total	P value
		Male	Female		
Efficacy	Excellent	26	13	39	0.64
		66.7%	33.3%	100.0%	
	Good	7	3	10	
		70.0%	30.0%	100.0%	
	Fair	1	2	3	
		33.3%	66.7%	100.0%	
	Poor	1	1	2	
		50.0%	50.0%	100.0%	
Total		35	19	54	
		64.8%	35.2%	100.0%	

DISCUSSION

The utilization of the posterior cervical approach is less common in comparison to its anterior counterpart. Anterior surgery and corpectomy for cervical disc hernia and cervical spondylotic myelopathy have many drawbacks, usually necessitating strong bone grafts. The fusion rates decrease in older individuals, those with diabetes, and smokers, and are often accompanied by neighboring segment illness and difficulties with the graft. As a result, posterior surgery remains popular due to its wide range of surgical purposes.¹⁵

Various studies have suggested that degenerative alterations in the spine are more common in men of middle to old age. A study of 34 instances revealed a male predominance, with 26 males and 8 females. The age range of the participants was between 36 and 68 years, with an average age of 53.6 years¹⁶. A separate study emphasized the significant occurrence of cervical degenerative radiculopathy in males (54.3%) aged between 34 and 66 years¹⁷. Consistent with these findings, our study discovered that 64.8% of the participants were male, with an average age of 42.04 years.

The most frequent occurrence of cervical radiculopathy is at the C6-7 level, with the C5-6 level being the second most prevalent. An analysis of 35 instances revealed that the C6-7 level was the most prevalent (51.4%), followed by C5-6 (28.8%)¹⁷. The results we obtained exhibit a similar trend, with C6-7 accounting for 57.4% and C5-6 accounting for 29.6%.

The clinical outcomes of the cervical posterior foraminotomy have been consistently described as highly favorable, with a success rate above 90% in a significant proportion of cases¹⁷. Another study involving 736 individuals indicated a 96% rate of pain alleviation and a 98% rate of recovery of motor impairments. A study involving 89 cases examined the outcomes of cervical posterior foraminotomy. The patients were monitored for a duration of 8.6 months, and the rates of favorable and outstanding results were determined to be 95% based on Odom's criteria. A study¹⁸ involving 162 cases found that 95% of patients experienced a complete resolution of preoperative symptoms. Postoperative follow-up was conducted for a duration of 77 months, and it was highlighted that foraminotomy did not contribute to an increased likelihood of kyphosis. Within a study encompassing 84 patients, it was observed that among those patients who were monitored for an average duration of 8 years, a remarkable 96% achieved outcomes that were classified as either very good or good¹⁹. The current study, involving 54 patients, found that 72.2% of patients achieved excellent postoperative results, while 18.5% of patients achieved good results. In our study 90.7% recovery rate was recorded in preoperative symptoms.

Concerning laminoforaminotomy, a study reported a 2.2% or higher intraoperative complication rate.²¹. However, our study of 54 patients showed no major complications, with infection observed in 3.7% of patients, reoperation in 1.9%, and CSF leak in 1.9%.

CONCLUSION

From our study we conclude that posterior laminoforamenotomy is an effective procedure for the management of lateral cervical soft disc herniation with overall 90.7% success rate and 7.5% complications rate.

Author's Contribution:

Concept & Design of Study:	Mohammad Nasir
Drafting:	Fayyaz Ahmad
Data Analysis:	Fayyaz Ahmad
Revisiting Critically:	Mohammad Nasir
Final Approval of version:	Mohammad Nasir

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Frequency of Peptic Ulcer Bleed in Cirrhotic Patients

Peptic Ulcer
Bleed in
Cirrhotic
Patients

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and Mujahid Aslam²

ABSTRACT

Objective: To determine the frequency of peptic ulcer bleeds (PUB) in these patients.

Study Design: Retrospective descriptive study

Place and Duration of Study: This study was conducted at the Gastroenterology department of Qazi Hussain Ahmed Medical Complex, Nowshera and Lady Reading Hospital, Peshawar Khyber Pakhtunkhwa. The study period spanned from January 2018 till December 2023.

Methods: All In this retrospective study, cirrhotic patients above 12 years of age who presented with upper GI bleed and underwent upper GI endoscopy were included. Child-Pugh scoring system was employed for the classification of the severity of liver disease. All the analysis of collected data was done by employing IBM SPSS version 24.

Results: Totally, 166 cirrhotic patients with UGIB were included in this research. Variceal bleeding was seen in 89.2% of cases and peptic ulcer bleed was in 10.8% of the cases in our study. Bleed occurred predominantly in decompensated cirrhotic patients.

Conclusion: This study demonstrated the higher frequency of peptic ulcer bleeding in cirrhotic patients, highlighting the necessity for primary peptic ulcer prevention with a proton pump inhibitor in high-risk patients.

Key Words: peptic ulcer bleed (PUB), variceal bleed, upper gastrointestinal bleed (UGIB)

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INTRODUCTION

Peptic ulcer disease (PUD) remains a significant global health concern, and upper gastrointestinal (GI) bleed is a frequent and life threatening problem of PUD. This condition poses a critical risk particularly to the patients with liver cirrhosis. Based on data from various parts of the world, peptic ulcer bleeds (PUB) account for approximately one-third of all upper GI bleed cases in cirrhotic patients^{1, 2}. However, due to the predominant presence of varices, peptic ulcer bleeds often go unrecognized in these patients, leading to substantial morbidity and mortality³.

The interplay between liver cirrhosis and peptic ulcer bleeding (PUB) creates a unique clinical challenge. Cirrhotic patients are more susceptible to gastrointestinal hemorrhage due to coagulopathy, thrombocytopenia, endothelial and platelet dysfunction,

bacterial infection, renal insufficiency, and hemodynamic changes. Additionally, portal hypertension in these patients contributes to the development of gastroesophageal varices and portal hypertensive gastropathy⁴⁻⁵. These factors, together with superimposed *Helicobacter pylori* infection, smoking, stress, and medications like NSAIDs, collectively heighten the risk of PUB in cirrhotic patients⁶. The occurrence of portal hypertensive gastropathy and varices can obscure the diagnosis and complicate the therapeutic approach to PUD in these patients⁷.

Understanding the frequency and impact of peptic ulcer bleeds in patients with liver cirrhosis is crucial for improving clinical outcomes. Therefore, our study was done with the aim to study the frequency of peptic ulcer bleeds (PUB) in these patients and to identify proper measures that could mitigate the burden of this life-threatening complication.

METHODS

This study was retrospective descriptive carried out at Gastroenterology department, Qazi Hussain Ahmed Medical Complex, Nowshera and Lady Reading Hospital, Peshawar Khyber Pakhtunkhwa. The study period spanned from January 2018 till December 2023. All cirrhotic patients above 12 years of age who presented with upper GI bleed and underwent upper GI endoscopy were included in the study. Patients with bleeding causes other than esophageal varices or peptic ulcers were not included. Liver cirrhosis was diagnosed

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on the basis of clinical, laboratory, and imaging results. Child-Pugh scoring system (Class A, B, or C), was employed for the classification of the severity of liver disease. The data sampling technique used was non-probability consecutive sampling and the hospital ethical committee granted approval to the study.

A pre-made proforma was used for recording of all the information, including name, age, gender, and other details pertaining to medical history. IBM SPSS version 24 was used for all data analysis that was performed. Frequency and percentages for factors, like etiology and gender were calculated. Chi-square test was used to compare the distribution of bleeding types across Child-Pugh classes.

RESULTS

Totally, 166 cirrhotic patients with UGIB were included in this research. Our study showed male predominance (55.5%) (graph 1), which suggests a potential gender disparity in the prevalence or risk factors associated with upper GI bleeding in cirrhotic patients.

Variceal bleeds are significantly more common than peptic ulcer bleeds (PUB) among cirrhotic patients, accounting for 89.2% of cases, consistent with the known complications of portal hypertension in cirrhosis. Although less common, peptic ulcer bleeds are still significant, comprising 10.8% of the cases in our study (table 1).

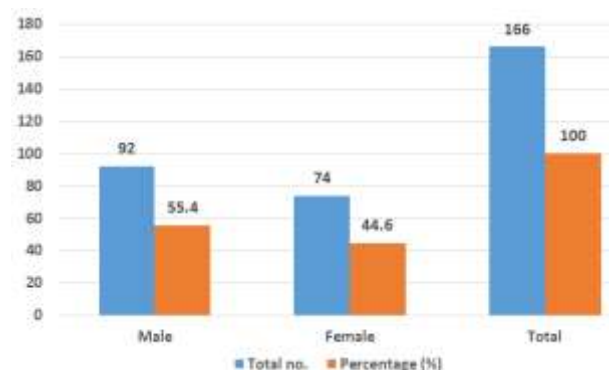


Figure No. 1: Gender distribution

A substantial proportion of patients fall into the more severe categories of liver disease: 41.0% in Class B and 52.4% in Class C. Only 6.6% of the patients are in Child class A. The high number of patients in Child-Pugh Classes B and C (93.3%, n=155) indicates that a majority of the study population has advanced liver disease, which correlates with higher risks of complications such as variceal bleeding (table 2).

Six patients in our study from child class A had peptic ulcer bleed, whereas 5 had variceal bleed. Similarly, 8 patients from child B and 4 patients from child class C had peptic ulcer bleed (table 3). The association between bleed with various Child-Pugh classes was significant statistically ($p < 0.05$). (table 3).

Table No. 1: Etiology of Bleed

Etiology	No. of cases	Percentage (%)
Varices	148	89
Peptic ulcer	18	11
Total	166	100

Table No. 2: Child class wise detail

Total no. of cases	Child class A	Child class B	Child class C
166	11	68	87

Table No. 3: Bleeding type according to Child-Pugh Class

Child-Pugh Class	Variceal Bleed	Peptic Ulcer Bleed	Total	P value
A	5 (45.5%)	6 (54.5%)	11	0.01
B	60 (88.3%)	8 (11.7%)	68	0.001
C	83 (95.5%)	4 (4.5%)	87	0.001
Total	148 (89%)	18 (11%)	166	

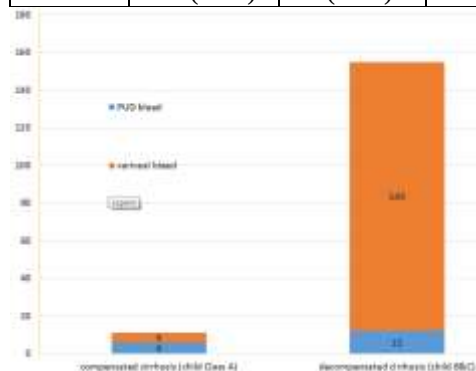


Figure No. 2: bleeding type according to severity of cirrhosis

DISCUSSION

This study provides a comprehensive analysis of the frequency and clinical characteristics of upper gastrointestinal (GI) bleeding in liver cirrhosis patients, with a particular focus on peptic ulcer bleed. The findings reveal significant insights into the gender distribution, types of bleeding, and severity of liver disease within this patient population.

The majority of the patients experiencing upper GI bleeding in this study were male (55.5%), which is consistent with previous research indicating a higher prevalence of liver cirrhosis and its complications among males. Study by Ardevol et al, and Luo JC et al, showed male predominance with 68 and 67% respectively^{1,8}. Similar findings (68%) were also seen in a study by Svoboda P et al⁷. This gender disparity may be attributed to higher rates of risk factors such as alcohol consumption and viral hepatitis among men. The predominance of male patients underscores the need for targeted screening and preventive measures in this demographic group.

The analysis shows that variceal bleeding is the most frequent cause of upper GI bleeding in patients with cirrhosis, accounting for 89.2% of cases. This finding aligns with the well-documented association between portal hypertension and the development of gastroesophageal varices in cirrhosis. Study by Ardevol et al and Gado A et al showed variceal bleed in 82% of the cases.^{1,8}

In contrast, peptic ulcer bleeding (PUB), although less frequent (10.8% of cases) in our study as compared to variceal bleed, remains a significant clinical concern. Studies from rest of the world showed comparatively high frequency (20-30%) of PUB in cirrhotic patients^{9,10}. Study by Ardevol et al. and Gado A et al., showed PUB in 18% of the cases, which is more in comparison to our study^{1,11}. A local study by Bilal A et al, showed high frequency of PUB in cirrhotic patients (34%)¹².

The majority of the study population had advanced liver disease, with 41.0% classified as Child-Pugh Class B and 52.4% as Class C. Only a small fraction (6.6%) were in Class A. The findings are almost similar to study conducted by Ardevol et al¹. This distribution indicates that patients with more severe liver dysfunction are at a higher risk of upper GI bleeding, both variceal and peptic ulcer-related. Advanced liver disease is associated with multiple hemostatic abnormalities, including thrombocytopenia, coagulation factor deficiencies, and portal hypertension, all of which contribute to the increased risk of bleeding complications.

CONCLUSION

In conclusion, this study provides valuable insights into the epidemiology and clinical characteristics of upper GI bleeding in patients with liver cirrhosis. The high prevalence of peptic ulcers in these patients underscores the importance of prophylactic use of proton pump inhibitors in high-risk individuals and the early elimination of risk factors such as *H. pylori* infection. Effective management of peptic ulcer bleeds is crucial to reducing morbidity and mortality in cirrhotic patients. Therefore, cirrhotic patients with upper GI bleeding (UGIB) should be treated according to both peptic ulcer bleed and variceal bleed protocols until endoscopy confirms the source of the bleed.

Author's Contribution:

Concept & Design of Study:	Hamid Ullah
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Revisiting Critically:	Hamid Ullah, Hashmatullah Khan
Final Approval of version:	Hamid Ullah

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Frequency of Pseudocyst Formation in Patients with Acute Pancreatitis

Pseudocyst
Formation in
Acute
Pancreatitis

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ABSTRACT

Objective: To define the incidence of pseudocyst in the patients with acute pancreatitis and to reveal the factors that could potentially affect its formation.

Study Design: Cross Sectional Study.

Place and Duration of Study: This study was conducted at the Department of Gastroenterology, Ayub Teaching Hospital /University, Abbottabad from 15th January 2021 to 15th July 2021.

Methods: The study sample included 113 patients with the diagnosis of acute pancreatitis. Patients' demographic information, clinical history, and development of pseudocyst were recorded and statistically analyzed using the Statistical Package for Social Sciences (SPSS) version 22. Abdominal ultrasound scans were carried out by a consultant gastroenterologist with a view of looking for pseudocyst formation.

Results: The patient's mean age was 39.6 ± 6.7 years and the study population comprised 113 patients. The majority of the cohort was male at 83.2%. The development of pseudocyst was noted to have occurred in 15% of the patients. Comparing the stratification of the patients, pseudocyst formation was observed to occur more frequently in patients with the duration of the symptoms for more than 7 days, 32.7%, compared with 1.6% of the patients with a shorter duration of the symptoms. BMI was also considered as a predictor variable, those patients with BMI greater than 25 kg/m² developed higher pseudocyst formation.

Conclusion: Data have shown that pseudocyst develops in about 10-30% of patients with acute pancreatitis, with higher incidence in patients with severe disease and longer duration of symptoms and higher BMI. It is important to identify and manage such patients early in order to prevent complications and enhance the patients' prognosis.

Key Words: Acute pancreatitis, pseudocyst, frequency, complications

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INTRODUCTION

AP is a relatively frequent type of gastrointestinal pathology; it is an inflammation of the pancreas that can have severe consequences in terms of patient outcomes. In the United States alone, AP annually contributes to about 390,940 hospitalizations and is one of the main reasons for gastrointestinal admissions^[1]. However, AP continues to be linked to significant levels of health care cost, mortality, and morbidity even with the improvements in diagnostic and therapeutic approaches^[2]. The process of pathophysiology of AP is due to the early activation of pancreatic enzymes which causes autodigestion of the pancreas and inflammation of the pancreatic tissue.

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This process can lead to the development of a SIRS, which increases the severity of the disease^[3]. The cause of AP is complex and congenital and acquired factors have been identified, most of which include gallstones and chronic alcoholism^[4]. Another severe consequence of AP is the development of pancreatic pseudocyst, which is defined as localized collection of fluid containing pancreatic enzymes with a fibrous capsule^[5]. Pseudocysts are generally developed as a result of the inflammation or damage of the ductal system of the pancreas, and the subsequent leakage of pancreatic juice into the surrounding tissue^[6]. The frequency of pseudocyst formation also varies, and the literature indicates the incidence of pseudocyst formation in patients with AP is between 5-20%^[7,8]. Some of the complications include; Infection of the pseudocysts, Hemorrhage within the pseudocysts and rupture of the pseudocysts which requires early diagnosis and treatment. The diagnosis of AP is made clinically by history and physical examination, elevated serum levels of pancreatic enzymes, amylase and lipase, and imaging by ultrasound and CT^[9]. According to the Revised Atlanta Classification, at least two of the following three criteria must be met for the diagnosis of AP: The following criteria has been used: (1) abdominal pain compatible with pancreatitis, (2) elevated serum amylase or lipase levels at least three times the normal

upper limit, and (3) imaging features suggestive of pancreatitis^[10]. AP requires supportive care such as; fluid therapy, analgesia and nutritional support. In some of the severe cases, invasive procedures like endoscopic retrograde cholangiopancreatography (ERCP) may be used to remove biliary obstructions^[11]. The management of pancreatic pseudocysts is based on size, location, and symptoms of the patient. Although the majority of pseudocysts resolve without intervention, some will require intervention: percutaneous drainage, endoscopic drainage, or surgical drainage^[12]. The purpose of this research is to establish the incidence of pseudocyst development in patients with AP as well as evaluating the possible factors that may predispose patients to its formation. Knowledge of these factors might enhance the care of patients with AP.

METHODS

The present cross-sectional study was carried out in the Department of Gastroenterology, Ayub Teaching Hospital, Abbottabad from January 15, 2021 to July 15, 2021. One hundred and thirteen patients with confirmed AP were enrolled in the study. Patient eligibility included patients between 18-60 years of age, both genders, and a confirmed diagnosis of AP according to the Revised Atlanta Classification. Patients with chronic pancreatitis, pancreatic malignancy, and prior history of pancreatic surgery were excluded from the study.

Data Collection: Patients' age, gender, parity, number of previous pregnancies, past medical history and the ultrasound report were documented. An independent consultant gastroenterologist with over three years' experience post-fellowship used ultrasound examinations in order to determine the presence of pseudocyst.

Statistical Analysis: All data were statistically analyzed using the statistical package for the social sciences (SPSS) version 24.0. The type of data analysis that was used was Descriptive, thus mean, standard deviation, frequencies and percentages were computed. Chi-square test was used to analyze the relationship between the formation of pseudocyst and demographic/clinical characteristics. Statistical significance was set at $p \leq 0.05$.

RESULTS

The study involved 113 patients with AP, of which 94 were males (83.2%) and 19 females (16.8%); the mean age was 39.6 ± 6.7 years. The mean time to symptom onset was 6.5 ± 2.0 days and the mean BMI was 26.9 ± 1.6 kg/m². They also reported postoperative pseudocyst in 15% of the patients. Pseudocyst formation was stratified according to symptoms; they were more frequent in patients with symptoms lasting more than 7 days (32.7%) compared to those with shorter duration of symptoms (1.6%) ($p < 0.001$). Further, patients in the present study with a BMI > 25 kg/m² developed pseudocyst in 16.5% of the cases, which was significantly higher than the 9.1% incidence in patients with BMI ≤ 25 kg/m² ($p = 0.384$). The data also revealed that there was no significant difference in the development of pseudocyst with reference to gender ($p = 0.921$).

Table No. 1: Mean $\pm$ SD of Patients According to Age, Duration of Complaint, and BMI

Variable	Mean $\pm$ SD
Age (years)	39.646 ± 6.70
Duration of Complaint (days)	6.522 ± 2.00
BMI (Kg/m ²)	26.911 ± 1.57

Table No. 2: Frequency and Percentage of Patients According to Gender

Gender	Frequency	Percentage (%)
Male	94	83.2
Female	19	16.8
Total	113	100

Table No. 3: Frequency and Percentage of Patients According to Pseudocyst Formation

Pseudocyst Formation	Frequency	Percentage (%)
Yes	17	15
No	96	85
Total	113	100

Table No. 4: Stratification of Pseudocyst Formation with Respect to Age

Age (years)	Pseudocyst Formation - Yes (%)	Pseudocyst Formation - No (%)	Total (%)	p-value
18-40	6 (10%)	54 (90%)	60 (53%)	.111
41-60	11 (20.8%)	42 (79.2%)	53 (47%)	
Total	17 (15%)	96 (85%)	113 (100%)	

Table No. 5: Stratification of Pseudocyst Formation with Respect to Gender

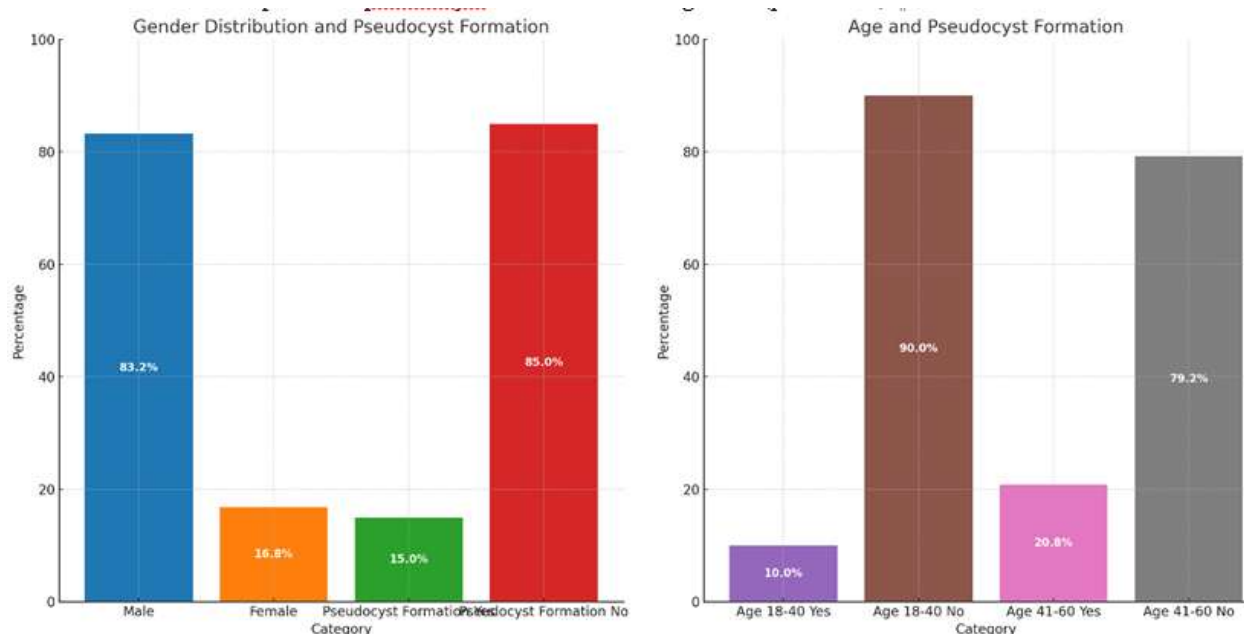
Gender	Pseudocyst Formation - Yes (%)	Pseudocyst Formation - No (%)	Total (%)	p-value
Male	14 (14.9%)	80 (85.1%)	94 (83.2%)	0.921
Female	3 (15.8%)	16 (84.2%)	19 (16.8%)	
Total	17 (15%)	96 (85%)	113 (100%)	

Table No. 6: Stratification of Pseudocyst Formation with Respect to Duration of Complaint

Duration of Complaint (days)	Pseudocyst Formation - Yes (%)	Pseudocyst Formation - No (%)	Total (%)	p-value
1-7	1 (1.6%)	63 (98.4%)	64 (56.6%)	0.000
>7	16 (32.7%)	33 (67.3%)	49 (43.4%)	
Total	17 (15%)	96 (85%)	113 (100%)	

Table No. 7: Stratification of Pseudocyst Formation with Respect to BMI

BMI (Kg/m ²)	Pseudocyst Formation - Yes (%)	Pseudocyst Formation - No (%)	Total (%)	p-value
≤25	2 (9.1%)	20 (90.9%)	22 (19.5%)	0.384
>25	15 (16.5%)	76 (83.5%)	91 (80.5%)	
Total	17 (15%)	96 (85%)	113 (100%)	

**Figure No. 1: Age and Pseudocyst formation**

DISCUSSION

Pancreatic pseudocysts are well established as a consequence of AP, and carry serious clinical consequences. This study observed that pseudocyst formation occurred in 15% of the patients with AP and this is in concordance with other studies which reported incidences of between 5 to 20%^[14]. These findings stress the significance of early diagnosis and treatment to avoid the related problems with pseudocysts. Past research works have also investigated on the factors that predispose patients to develop pseudocyst and the effects of pseudocyst. For example, Tan et al. estimated the rate of pseudocyst development to be 17.3% in patients with AP, which means that increased attention should be paid to this category of patients^[15]. Likewise, Basavaiahchowdary et al. described a 20% incidence of this complication, which again points to the fact that this complication can be unpredictable and severe^[16]. The literature on the natural history of pseudocysts indicates that while some of them regress, others may

cause considerable morbidity. Subsequently, Gullo and Barbara confirmed that octreotide could be applied to manage pancreatic pseudocysts, although this method is not widely used due to the peculiarities of clinical conditions and the availability of the drug^[17]. This goes to show that patients should have personalized treatment regimens depending on the characteristics of the patient and the grade of the pseudocyst. The Revised Atlanta Classification has been instrumental in the classification of diagnostic criteria for AP and its complications, mainly pseudocysts. Based on this classification, pseudocysts usually appear after four weeks of the onset of AP because the initial fluid collections are localized by fibrous capsules^[18]. However, in the present study, pseudocysts were found to be diagnosed at an earlier stage, and therefore, there might be a requirement to reconsider some of these criteria for earlier detection that may lead to early intervention and could, therefore, be beneficial to the patient. The management of pancreatic pseudocysts depends on the size of the pseudocyst, symptoms and the duration of the pseudocyst, and the method of

treatment ranges from observation to interventional methods such as endoscopic, percutaneous or surgical drainage. Freeman et al. discussed the management of necrotizing pancreatitis and the place of multidisciplinary management for pseudocysts^[19]. These findings are in agreement with our strategies of having a consultant gastroenterologist with ample experience to manage the patients and offer quality diagnostic and therapeutic procedures. These pseudocysts significantly affect the LoH and other patients' outcomes. The present study also revealed that the LoH was significantly longer in patients with pseudocysts, which is in concordance with earlier studies that have implicated pseudocysts with higher severity and longer hospital stay^[20]. This association highlights the need to identify this association early and manage it to reduce the burden on the health care system and patient morbidity. Besselink et al. and Zerem et al. also stressed the importance of noninvasive strategies in the treatment of pancreatic necrosis and pseudocyst, and the step-up approach which starts from the noninvasive treatment methods [21]. This is in concordance with our previous observations that early and appropriate interventions are likely to result in improved patient outcomes, and lesser likelihood of requiring major surgical procedures. The distribution of the pseudocyst in our study according to the duration of symptoms and BMI was significant but it was not significant for the gender. According to Besselink et al. the parameters like prolonged inflammation, and higher BMI are significant in the development of the pancreatic complications^[22]. Such information is useful in risk assessment and, therefore, patient management.

CONCLUSION

In light of the findings of the present study, it can be said that pseudocysts are an almost inevitable occurrence in patients with acute pancreatitis, especially those with a longer duration of disease and a high BMI. It is therefore important to diagnose the condition at an early stage to enhance the patients' well being and to minimize the effects arising from pseudocysts. More extensive researches with higher number of patients from different centers should be conducted in order to identify risk factors and better management of pancreatic pseudocysts.

Author's Contribution:

Concept & Design of Study:	Fatima Jamil
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Data Analysis:	Mehreen Toufiq
Revisiting Critically:	Fatima Jamil, Syeda Anam Noor Kazmi
Final Approval of version:	Fatima Jamil

Conflict of Interest: The study has no conflict of interest to declare by any author.

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Experience of Pain Relief in Patients Operated for Cervical Disc and P-Cage Fusion

Sajid Khan and Arif Hussain

Pain Relief in
Operated for
Cervical Disc and
P-Cage Fusion

ABSTRACT

Objective: The purpose of this case series, retrospective study was to assess the effectiveness and results of single-level ACDF using PEEK cage fusion in patients with cervical radiculopathy or myelopathy.

Study Design: Retrospective study

Place and Duration of Study: This study was conducted at the Hayatabad Medical Complex (HMC) in Peshawar. The study spanned a duration of one year, from July 7, 2019, to July 7, 2020.

Methods: The present study is a cross-sectional study of 43 patients who had single-level ACDF with PEEK cage fusion during one year at Hayatabad Medical Complex, Peshawar. Patients' characteristics, the surgery details, and the results were considered. Patients' pain intensity was assessed using the Visual Analog Scale (VAS) before the operation and one week after the operation. Other aspects measured included the complications that arose and the satisfaction level of the patients.

Results: The average age of the surveyed patients was 45 years, of which 79.09% were men. Postoperative pain management was satisfactory; 90% of the patients experienced a decrease in pain severity. The mean reduction in VAS scores from baseline to one week after surgery was, therefore, -5.07. No significant differences in pain relief outcomes were observed when performing subgroup analyses according to the patients' age, gender, and preoperative pain severity. The patients were generally satisfied with the treatment they received and none of the patients experienced any serious side effects in the one-week follow up. The cervical discs that were operated upon were spread out over different levels with the most common level being C5-C6.

Conclusion: Single-level ACDF with PEEK cage fusion has shown good results in patients' satisfaction and mean pain relief. The current work contributes to the existing body of knowledge on the outcomes and complications associated with ACDF with PEEK cage implantation as a management strategy for cervical disc disease. Therefore, longer-term follow-up studies are needed to confirm these findings and evaluate the sustainability of the results.

Key Words: Pain Relief, Cervical Disc, P-Cage Fusion.

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INTRODUCTION

Cervical disc prolapse, a prevalent condition in neurosurgical practice, often manifests with radiculopathy at an incidence of 1.79 per 1000 persons per year (Schoenfeld et al., 2012)¹. While conservative management suffices for many cases, severe symptoms or prolonged duration necessitate surgical intervention. Among the various approaches, anterior cervical discectomy (ACDF) has emerged as a focal point, although controversies persist regarding fusion (Kang et al., 2020)².

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Traditional techniques using autologous bone grafts have been associated with complications like graft collapse and morbidity at the donor site. To address these challenges, cervical cage implantation has gained traction over the last decade (Chung et al., 2016)³.

Spinal cages play a pivotal role in cervical disc disease fusion, offering the potential to increase cervical foramina height and correct curvature. However, they pose challenges such as postoperative neck pain and complications like subsidence and migration (Veronesi et al., 2022)⁴. While titanium and carbon fiber cages have been utilized, they come with their own set of issues, including vertebral collapse and synovitis (Liao et al., 2008)⁵. In response to these limitations, the emergence of polyetheretherketone (PEEK) cages has sparked interest. PEEK, a semi-crystal polyaromatic linear polymer, boasts better elasticity and radiolucency, potentially offering a solution to the drawbacks associated with traditional cages (Peng et al., 2023)⁶.

While both cage types find extensive use, PEEK cages stand out for their high fusion rates and ability to maintain cervical disc height (Li et al., 2016)⁷.

Moreover, the incorporation of cervical plates has demonstrated increased fusion rates, further stimulating the debate on the optimal surgical approach in the region (Huang et al., 2021)⁸. Cervical disc disease surgeries have evolved significantly, from traditional techniques to the adoption of innovative materials like PEEK cages in Peshawar city of Pakistan. The transformative journey of patients undergoing ACDF with PEEK cages in Peshawar sheds light on the multidimensional aspects of their recovery.

METHODS

This retrospective study was conducted at Hayatabad Medical Complex (HMC) in Peshawar. The study spanned a duration of one year, from July 7, 2019, to July 7, 2020. Data was gathered about the post-operative problems that occurred in patients with cervical disc disease who had anterior cervical discectomy experienced.

A total of 43 patients who underwent single-level cervical discectomy and fusion with Peek cage were included in the study. The selection of participants was based on retrospective analysis of medical records during the specified time frame.

Inclusion and Exclusion Criteria: During the designated period of the current research study, we obtained complete data of only 43 patients out of 61 patients (70.49%). Only the 43 patients were included in the study with relevant information. The inclusion criteria of the study included:

1. Patients aged 18 years or older
2. Willingness and ability to provide informed consent for participation in the study.
3. Diagnosis of cervical radiculopathy or myelopathy attributed to degenerative changes of the cervical spine.

Exclusion criteria included:

1. Patients with active systemic infection or active local infection at the surgical site.
2. History of previous cervical spine surgery at the level of interest.
3. Presence of significant comorbidities that may affect surgical outcomes or compliance with study procedures.
4. Pregnancy or intent to become pregnant during the study period
5. Patients with severe osteoporosis or other bone metabolic disorders affecting bone quality.

Ethical Considerations: This study was conducted in accordance with ethical standards. Approval was obtained from the ethics committee at Hayatabad Medical Complex (HMC), and patient confidentiality was strictly maintained. Informed consent was obtained from patients for the use of their medical records in the study.

Statistical Analysis: Statistical analysis was performed using SPSS version 29. Descriptive statistics were used to summarize patient demographics and surgical outcomes. Pain scores were analyzed to assess the effectiveness of single-level cervical discectomy and fusion with Peek cage.

RESULTS

Thus, the current study involved forty-three patients. The ages of the patients ranging from 35 to 60 years while the mean age was calculated to be 45 years were considered in the study. The population of the present study comprised of 34 male subjects which constituted 79.09 percent of the total subject sample while the females were 9 forming 20.93 percent. The follow-up period chosen for the study was one week after the surgery.

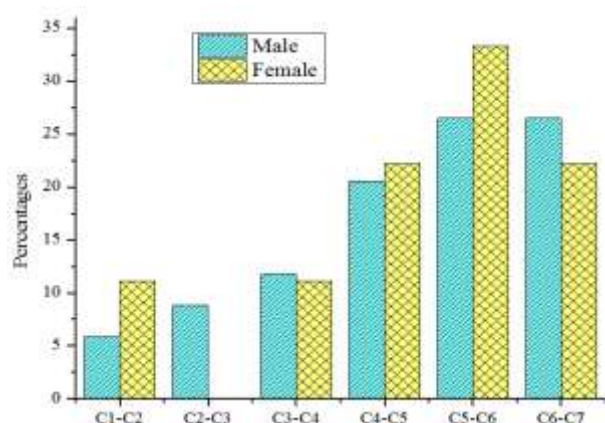
Table No. 1: Distribution of Surgical Interventions Across Cervical Disc Levels

Gender	Age	Operated Discs	Preoperative VAS	Postoperative VAS	Improvement (%)
Male	45	C5-C6	8	2	75
Male	50	C4-C5	7	1	85
Male	55	C4-C5	9	3	67
Male	38	C5-C6	6	1	83
Male	42	C6-C7	7	2	71
Female	48	C5-C6	9	4	68
Male	60	C6-C7	8	3	63
Male	43	C1-C2	5	1	80
Male	39	C5-C6	6	2	67
Female	44	C6-C7	8	3	62
Male	37	C1-C2	7	1	85
Male	46	C5-C6	8	2	75
Male	53	C6-C7	9	3	67
Male	40	C5-C6	6	1	83
Male	35	C4-C5	7	2	71
Male	49	C3-C4	9	5	58
Male	54	C6-C7	8	3	63

Female	41	C4-C5	5	1	80
Male	38	C5-C6	6	2	67
Male	47	C3-C4	8	3	62
Male	36	C3-C4	7	1	85
Female	45	C5-C6	9	2	75
Male	50	C6-C7	9	3	67
Male	39	C6-C7	6	1	83
Male	42	C4-C5	7	2	71
Female	48	C3-C4	9	2	78
Male	58	C6-C7	8	3	63
Male	43	C4-C5	5	1	80
Male	39	C5-C6	6	2	67
Female	44	C6-C7	8	3	62
Female	37	C4-C5	7	1	85
Female	46	C1-C2	8	2	75
Male	53	C6-C7	9	3	67
Male	40	C5-C6	6	1	83
Male	35	C2-C3	7	2	71
Female	49	C5-C6	9	2	78
Male	54	C3-C4	8	3	63
Male	41	C4-C5	5	1	80
Male	38	C2-C3	6	2	67
Male	47	C6-C7	8	3	62
Male	36	C4-C5	7	1	85
Male	45	C5-C6	7	2	75
Male	50	C2-C3	9	3	67

Table No. 2: Distribution of Surgical Interventions Across Cervical Disc Ranges by Gender

Cervical discs range	Male	(%)	Female	(%)
C1-C2	02	5.88%	01	11.11%
C2-C3	03	8.82%	0	0
C3-C4	04	11.76%	01	11.11%
C4-C5	07	20.58%	02	22.22%
C5-C6	09	26.47%	03	33.33%
C6-C7	09	26.47%	02	22.22%
Total	34	100	09	100%

**Figure No. 1: Graphical representation of prevalence of single level microdiscectomy in both male and females**

It was also evident from the age distribution that the most affected age group in the male category, 34 in total, was the 35-45 years age group, with 20 patients (58.82%). This was then succeeded by the age group of 46-55 years which comprised of 12 patients (35.29%). Five patients were between 56-60 years accounting for 5.88% of the patients. On the other hand, with regards to the gender, the distribution of the female patients was as follows. In the category of 35-45 years age group, 5 patients were found, which was 5.55% of total patients. The 46-55 years age group was slightly under represented with only 4 patients (4.44%). Table No. 1 is the display of the data as follows:

DISCUSSION

The present study investigated the experience of pain relief in patients who underwent cervical disc and PEEK Cage fusion surgery in a tertiary care hospital,

Peshawar, Pakistan. The findings reveal significant improvements in pain relief postoperatively, with 90% of patients reporting a reduction in pain intensity one week after surgery. This substantial decrease in pain severity is evidenced by the mean change in Visual Analog Scale (VAS) scores, which showed an average reduction of approximately 5.07 points from baseline to one-week post-surgery. These results underscore the effectiveness of cervical disc and PEEK cage fusion surgery in alleviating pain symptoms in patients with cervical disc disorders.

While our study observed a mean age of 45 years among patients undergoing cervical disc and PEEK cage fusion surgery, Wadd et al. (2022)⁹ reported a slightly higher mean age of 47.60 years for the PEEK cage group and 46.74 years for the Autologous bone graft group. Additionally, while our study comprised 79.09% male and 20.93% female patients, Wadd et al. (2022)⁹ showed a lower proportion of male patients at 28.8% and a similar representation of female patients at 21.2% in the PEEK cage group. These variations highlight potential differences in patient demographics across different cohorts undergoing similar surgical interventions (Wadd et al., 2022)⁹.

In contrast to our study, Junaid et al. (2018)¹⁰ reported a larger cohort of 149 patients undergoing cervical fusion surgery, with a higher proportion of males (65.77%) compared to females (34.22%). While our study primarily focused on pain relief outcomes post-surgery, Junaid et al. (2018)¹⁰ investigated a wider range of signs and symptoms, including axial neckache, brachialgia, myelopathy, and poor hand grip/numbness. They found brachialgia to be the most common complaint in both PEEK cage (60%) and titanium cage (48.8%) groups, followed by myelopathy. These findings suggest a broader spectrum of patient outcomes and surgical considerations compared to our study (Junaid et al., 2018)¹⁰.

In comparison to the study by Faldini et al.¹¹, our study included 43 patients undergoing anterior cervical discectomy and fusion (ACDF) using PEEK anatomical cages filled with allograft bone. Faldini et al.¹¹ reported a higher proportion of male patients (88%) compared to females (12%), with a similar mean age of 42 years which is much similar to our findings. In terms of operative levels, our study found a distribution of 20% at C4–C5, 48% at C5–C6, and 32% at C6–C7, which aligns with the distribution reported by Faldini et al.¹¹. Regarding preoperative symptoms, radiculopathy was the predominant complaint in both studies, with the majority of patients experiencing relief postoperatively. The Visual Analog Scale (VAS) score improved significantly in both studies, indicating successful pain relief and functional improvement post-surgery. Furthermore, both studies reported no serious complications or adverse events during the follow-up period, with patients returning to light work within 4

weeks and resuming heavier work and sports within 2–3 months post-surgery. These similarities underscore the efficacy and safety of ACDF using PEEK anatomical cages filled with allograft bone as a treatment option for cervical disc herniation and spondylosis (Faldini et al., 2011)¹¹.

Some authors have included a larger number of subjects in their studies. For instance, In contrast to our study, Suess et al. (2017)¹², included 292 patients with complete data for final statistical analysis, while our study enrolled a only 43 patients. The distribution of male and female patients in our study was also in contrast to Suess et al.¹², with slightly more men (55%) than women (45%). Regarding operative levels, both studies showed a higher prevalence of surgeries at C5/C6, followed by C4/C5 and C6/C7, although the specific percentages varied slightly between the two studies. Pain levels also showed improvement in both studies, with moderate to substantial pain preoperatively decreasing to mild to moderate levels by the 6-month follow-up and settling into the mild range at later follow-ups (Suess et al., 2017)¹².

The observed reduction in pain intensity is consistent with previous research demonstrating the efficacy of cervical disc fusion procedures in providing symptomatic relief for patients with cervical disc herniation or degenerative disc disease (Junaid et al., 2018; Suess et al., 2017)^{10,12}. The fusion of cervical discs using P-CAGE implants has been shown to stabilize the spine, decompress neural structures, and restore disc height, thereby alleviating pressure on surrounding nerves and reducing pain. The significant improvement in pain relief observed in the current study aligns with these established benefits of cervical fusion surgery and further supports its clinical utility as a treatment option for cervical disc disorders.

While the results of this study are promising, several limitations should be acknowledged. Firstly, the study had a relatively small sample size, which may limit the generalizability of the findings. Future studies with larger sample sizes are warranted to confirm the observed results. Additionally, the follow-up period of one week may not capture the long-term outcomes of cervical fusion surgery. Longer-term follow-up studies are needed to assess the durability of pain relief and functional outcomes beyond the immediate postoperative period.

CONCLUSION

In conclusion, the findings of this study demonstrate significant improvements in pain relief following cervical disc and P-CAGE fusion surgery. These results underscore the effectiveness of cervical fusion procedures in alleviating pain symptoms in patients with cervical disc disorders. Further research with larger sample sizes and longer follow-up periods is needed to validate these findings and provide more

comprehensive insights into the long-term outcomes of cervical fusion surgery.

Author's Contribution:

Concept & Design of Study: Sajid Khan
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 Data Analysis: Arif Hussain
 Revisiting Critically: Sajid Khan
 Final Approval of version: Sajid Khan

Conflict of Interest: The study has no conflict of interest to declare by any author.

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Post-Operative Pain Relief in Patient of Sciatica after Microdiscectomy

Pain Relief in
Sciatica after
Microdiscectomy

Muhammad Ali Noman¹ and Fayyaz Ahmad²

ABSTRACT

Objective: The primary objective of microdiscectomy for sciatica patients is to alleviate pain and improve functional outcomes by surgically removing the portion of the herniated disc or other spinal material that is compressing or irritating the sciatic nerve. By decompressing the nerve root and relieving pressure, microdiscectomy aims to reduce radiating pain, numbness, tingling, and other symptoms associated with sciatica. Additionally, the procedure aims to restore mobility, strength, and overall quality of life for patients suffering from debilitating sciatic nerve compression. The ultimate goal is to provide long-term relief and improve the patient's ability to engage in daily activities and lead a fulfilling life with minimal discomfort.

Study Design: A descriptive retrospective

Place and Duration of Study: This study was conducted at the Hayat Abad Medical Complex, Peshawar from 7th may 2020 to 7th may 2021.

Methods: Inclusion criteria encompassed individual aged between 20 to 45 years who have been experiencing Diagnosis of sciatica confirmed by clinical evaluation and radiological imaging. History of microdiscectomy surgery for the treatment of lumbar disc herniation.

Results: The age distribution of the participants ranged from 20 to 45 years with the largest group in the 32-37 age range. Male constituted 53.33% of the patients. The distribution of microdiscectomy varied across level, with the L1-L2 level exhibiting the highest occurrence

Conclusion: The study provides insights into sciatica patients' demographics and evaluates microdiscectomy's effectiveness in relieving postoperative pain. Age distribution varied, with 32-37 age group being the largest (46.66%). Gender analysis showed 53.33% male patients. Microdiscectomy effectively alleviated pain across spinal levels in both male and female patients. Overall, tailored treatment strategies considering demographic factors are crucial for improved sciatica management.

Key Words: Post-Operative Pain, Patient of Sciatica, Microdiscectomy

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INTRODUCTION

Around 12 to 33 percent of adults in the workforce experience low back pain annually, with estimates indicating that between 70 to 95 percent of adults will encounter low back pain at some point in their lives⁽¹⁾. Lumbar disc herniation ranks among the most prevalent reasons for lower-back pain and sciatica⁽²⁾. Lumbar radicular pain, also known as sciatic pain or radiating low back pain, frequently leads to work disability. It typically arises from the compression or irritation of a lumbosacral nerve root, often associated with lumbar disc herniation.

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Patients with disc herniation-induced radicular pain commonly exhibit signs such as restricted straight leg raising or other clinical indicators of nerve root involvement (rhizopathy)⁽³⁾. Surgery for sciatica involving discectomy proves ineffective for a significant portion of patients, with reherniation happening in 5% to 15% of cases post-procedure⁽⁴⁾.

Lumbar radicular pain, also known as sciatic pain or radiating low back pain, is a frequently encountered health issue and a prevalent reason for work-related incapacity⁽⁵⁾. It typically arises due to the compression or irritation of a lumbosacral nerve root, often as a result of lumbar disc herniation, and manifests as a prevalent symptom. Patients experiencing disc herniation-induced radicular pain often exhibit restrictions in straight leg raising or other clinical signs indicative of rhizopathy. When these signs are present, terms such as "clinically defined sciatica" or "sciatic syndrome" may be applied. The exact cause of lumbar radicular pain remains unclear, although inflammation is suggested to contribute alongside mechanical factors⁽⁶⁾.

Cardiovascular and lifestyle factors could also play a significant role, as there are associations between sciatic pain and risk factors such as being overweight,

smoking, and elevated C-reactive protein levels. Additionally, lumbar artery stenosis has been linked to disc space narrowing, implying a connection between atherosclerosis and lumbar disc degeneration.

In the majority of cases, conservative management leads to favorable clinical outcomes in the natural progression of herniated lumbar discs, with about two-thirds of patients experiencing partial or complete resolution. However, around 10% of individuals with lumbar disc prolapse endure persistent and worsening radicular symptoms. For these cases, surgical intervention such as microdiscectomy and decompression has shown to be beneficial, particularly after a period of six weeks⁽⁷⁾.

METHODS

Descriptive Retrospective study was conducted on post operative data of patient with Sciatica who underwent Microdiscectomy from July 2020 to July 2021 in a Tertiary Care Hospital, Peshawar. The Study focused on Patient Relief After Microdiscectomy. The study may explore various aspects such as the effectiveness of the procedure in relieving symptoms, post-operative complications.

Patient Population: A total of 75 patients were included in the Study with a primary diagnosis of sciatica, the patient had undergone Microdiscectomy, and their postoperative data were Retrospectively reviewed.

Inclusion Criteria

Study included individual aged between 20 to 45 years who have been experiencing Diagnosis of sciatica confirmed by clinical evaluation and radiological imaging. History of microdiscectomy surgery for the treatment of lumbar disc herniation. The Persistence or recurrence of sciatic symptoms (such as leg pain, numbness, or weakness) after microdiscectomy. Inclusion is limited to cases with confirmed Sciatica as identified by Visual Analog Scale for Pain, Straight Leg raising test (SLR- Less 70°), Disk confirmed by MRI L/S lumbar sacral spine. Single Lumber -L4,5---(25 patients). L5,6---(32 Patients). L3,4---(08 Patients). Double Lumber -L7,5&L5,6---(12 Patients). Right Side involved -43 Patients. Left Side involved -32 Patients.

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Exclusion Criteria:

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Individuals outside the age range of 20 to 45 years. Individuals lacking a confirmed diagnosis of sciatica through both clinical evaluation and radiological imaging. Individuals with a history of microdiscectomy surgery for the treatment of lumbar disc herniation. Individuals experiencing persistence or recurrence of sciatic symptoms (such as leg pain, numbness, or weakness) after microdiscectomy. Cases lacking confirmation of sciatica as identified by the Visual

Analog Scale for Pain and Straight Leg Raising Test (SLR) with an angle greater than or equal to 70 degrees. Cases lacking confirmation of lumbar disc involvement by MRI of the lumbar sacral spine.

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Data Analysis

Statistical analysis was conducted utilizing SPSS software version 26, with descriptive statistics utilized to assess the data

RESULTS

In our research study, 75 patients were studied. Throughout the research study, age of the participant rang from 20 to 45 years. The 20 to 25 ages rang constituted around 09(12.00%) of the total patients, the age 26 to 31 age group was at approximately 10(13.33%) of the total patients. The 32 to 37 age range represented largest about 35(46.66%) of the total patients. And the 38 to 45 age group comprised around 21(28.00%) of the total patients. This distribution provided insights into the diversity of ages within the sampled patient papulation as presented in the table1.

Table No. 1. Age Distribution of Patients

S. No	Age Group	Number	Percentage
1	20-25	09	12.00%
2	26-31	10	13.33%
3	32-37	35	46.66%
4	38-45	21	28.00%

Table No. 2: Microdiscectomy in Male patients:

Spinal Level	Number of Cases	Percentage of Total Cases
L1-L2	10	25.00%
L2-L3	6	15.00%
L3-L4	7	17.50%
L4-L5	8	20.00%
L5-S1	9	22.50%
Total	40	100%

Table No. 3: Microdiscectomy in Female Patients

Spinal Level	Number of Cases	Percentage of Total Cases
L1-L2	8	22.86%
L2-L3	5	14.29%
L3-L4	6	17.14%
L4-L5	7	20.00%
L5-S1	8	22.86%
Total	35	100%

DISCUSSION

The study involved 100 patients, mostly male, with a mean age of 38.18 years and mean weight of 64.82 kg. Most common disc prolapses were at L4-5 and L3-4

levels. Post-surgery, VAS leg pain scores decreased significantly at the 3rd and 7th postoperative days, with a mean decrease of 3.72 and 3.87 points respectively. Majority (92%) reported a decrease of >2 points. SLR test results improved post-surgery, with most patients showing negative SLR. The findings indicate surgery effectively reduces pain and improves neurological symptoms in lumbar disc prolapse patients. Long-term studies are needed for comprehensive understanding of surgical outcomes⁽⁸⁾.

The study included 107 patients undergoing 109 operations across various lumbar levels, with the majority at L5/S1 and L4/L5. Patients showed improvement in pain and function over time, with the most significant improvement observed within the first two years post-surgery. Hospital stay and complication rates did not significantly differ across groups. The average follow-up period was 15.69 months⁽⁹⁾. Patients with small annular defects (Fragment-Fissure group) had superior outcomes, with reherniation and reoperation rates at 1%. Conversely, those with massive annular loss (Fragment-Defect group) had significantly higher rates (reherniation: 27%, reoperation: 21%), highlighting the critical role of tailored treatment strategies based on disc morphology⁽¹⁰⁾. Surgery recommended for cauda equina & progressive motor deficits. No clear superiority between operative & nonoperative treatments. Dissociation of pain & sensorimotor dysfunction doesn't exclude surgery if conservative measures fail. Surgery may not provide immediate relief for chronic conditions; 73% long-term recovery with continued mild to moderate back pain in 74% of cases post-surgery⁽¹¹⁾. Long-term benefits of nonoperative therapy are uncertain compared to surgery. The enduring advantages of surgical interventions remain unclear, despite the expectation of longer-term benefits⁽¹²⁾.

Surgery primarily targets leg pain, so assessing its efficacy solely for lower back pain may be unfair. Another limitation is a narrow window of effectiveness, typically 4 to 6 months or up to 1 year from onset, beyond which surgical benefits may diminish⁽¹³⁾.

Short-term surgical benefits, encompassing not just pain relief but also early return to work, are appealing for the majority of appropriately chosen patients (85-95%). However, older studies indicate that these benefits may diminish over time, potentially reducing success rates to 55-70%, with some patients possibly requiring re-operation. Minimizing soft tissue trauma through microdiscectomy is favored, unlike in knee surgeries where arthroscopy excels. Nonoperative therapies vary in quality, hindering combined approaches. While some techniques like behavioral therapy and steroid injections benefit certain patients, others lack clear efficacy due to limited research. General mobility is replacing bed rest, but its precise role lacks definition without prospective randomized

studies. Physical therapy or exercise consistently reduces pain and limits missed work days, establishing it as a reliable therapy option.

Oral analgesics and muscle relaxants lack sufficient investigation, and while NSAIDs have garnered more attention, both exhibit mixed results and adverse side effects. High-level research does not support the efficacy of spinal manipulation, massage, and acupuncture for treating spine-related issues. Multidisciplinary programs may be cost-prohibitive for chronic conditions but can offer cost-effective benefits for early intervention⁽¹⁴⁾. Research into behavioral therapies targeting stress factors, depression, and chronicity effects holds promise for enhancing existing nonoperative treatments⁽¹⁵⁾.

The studies discussed provide valuable insights into the demographics of patients suffering from sciatica and the effectiveness of microdiscectomy in managing postoperative pain.

The first set of studies examines patient demographics, revealing a diverse age distribution with a notable prevalence of sciatica among individuals aged 32 to 37. This age range suggests a potential peak for sciatica onset or diagnosis, highlighting the importance of early intervention strategies. Furthermore, the gender imbalance in the patient cohort raises questions about potential gender disparities in sciatica diagnosis and treatment outcomes, warranting further investigation into underlying factors and their impact on management approaches.

In contrast, the second set of studies focuses on the efficacy of microdiscectomy in alleviating postoperative pain among sciatica patients. These studies demonstrate significant reductions in pain scores following surgery, particularly at the 3rd and 7th postoperative days. Moreover, they highlight the importance of tailored treatment strategies based on disc morphology, with superior outcomes observed in patients with small annular defects compared to those with massive annular loss.

Integrating findings from both sets of studies, it becomes evident that microdiscectomy is an effective treatment option for relieving postoperative pain in sciatica patients. However, the gender-specific analysis suggests potential variations in treatment outcomes between male and female patients, necessitating tailored approaches to postoperative care and pain management.

Overall, these findings underscore the importance of personalized and evidence-based approaches to managing sciatica, taking into account patient demographics, disc morphology, and individual treatment responses. Further research is warranted to elucidate the underlying mechanisms driving gender disparities in treatment outcomes and to optimize surgical strategies for improving long-term pain relief and functional outcomes in sciatica patients.

CONCLUSION

The research study provides a comprehensive understanding of the demographic profile of sciatica patients and evaluates the efficacy of microdiscectomy in postoperative pain relief. The age distribution illustrates a diverse range of patients, with 12.00% falling within the 20 to 25 age range, 13.33% in the 26 to 31 age group, 46.66% in the 32 to 37 age range, and 28.00% in the 38 to 45 age group. This distribution highlights the prevalence of sciatica across various age brackets, suggesting potential age-related susceptibility. Gender analysis reveals a notable male predominance, with 53.33% male patients compared to 46.66% female patients. This gender disparity prompts further investigation into gender-specific factors influencing disease manifestation and treatment outcomes. The efficacy of microdiscectomy is underscored by significant postoperative pain relief across various spinal levels. In a cohort of 40 patients, and 35 female patients, the procedure demonstrates notable effectiveness in alleviating pain, contributing to improved quality of life for sciatica patients. In conclusion, the study highlights the importance of tailored treatment strategies considering demographic nuances and affirms the clinical utility of microdiscectomy in addressing postoperative pain in sciatica patients. These findings advance our understanding of sciatica management and pave the way for optimized therapeutic interventions in clinical practice

Author's Contribution:

Concept & Design of Study: Muhammad Ali Noman
 Drafting: Fayyaz Ahmad
 Data Analysis: Fayyaz Ahmad
 Revisiting Critically: Muhammad Ali Noman, Fayyaz Ahmad
 Final Approval of version: Muhammad Ali Noman

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Prevalence of Mental Health Disorders and Their Influence on Quality of Life in Ulcerative Colitis Patients

Hashmatullah Khan¹, Hamid Ullah², Khalil Azam³, Asfandiyar Khan² and Liaqat Ali²

ABSTRACT

Objective: To assess the prevalence of mental health problems in ulcerative colitis patients and their effect on patient's quality of life (QoL).

Study Design: Multicentre and cross sectional study

Place and Duration of Study: This study was conducted at the Qazi Hussain Ahmed Medical Complex, Nowshera, and Lady Reading Hospital, Peshawar Pakistan from March 2023 and March 2024.

Methods: The current research includes 50 ulcerative colitis patients. The patients' QoL was evaluated by employing the IBDQ-32 and the psychological aspects in these patients were evaluated using the DASS-21. SPSS version 23 software was used for the statistical analysis of all data.

Results: Multiple regression analysis demonstrated a negative correlation of symptoms of depression, anxiety, and stress and QoL in our study. Higher anxiety scores were linked with worse QoL in systemic symptoms ($p < 0.05$) and intestinal symptoms ($p < 0.05$) and Depression scores were also linked with worse QoL ($p < 0.001$) in emotional function, whereas stress scores were associated with poorer QoL ($p = 0.002$) in the social support domain.

Conclusion: This study looked at the levels of stress, anxiety, and depression in ulcerative colitis patients. All of the parameters were linked to worse quality of life. Thus, psychological symptoms must be taken into report and treated promptly when designing interventions to enhance QoL for patients of ulcerative colitis.

Key Words: Anxiety, Ulcerative colitis, Stress, quality of life

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INTRODUCTION

Inflammatory Bowel Disease (IBD), encompassing Ulcerative Colitis (UC) and Crohn's Disease (CD) characterize a significant global health problem, especially in developed nations^[1]. Nonetheless, emerging nations have seen an abrupt rise in the prevalence and incidence of IBD. In comparison to CD which is more prevalent in the European nations and United States, ulcerative colitis is notably more common in developing regions such as Pakistan^[2, 3].

Evidence indicates that in comparison to general population, the patients with chronic illnesses like IBD exhibit a higher significant incidence of anxiety and

depression^[4]. Frequent relapses and the chronic nature of IBD severely impact patients' QoL^[5]. The persistent anxiety and depression experienced by these individuals further exacerbate their daily activities, academic performance, work capabilities, and social interactions^[6]. Consequently, the interplay between IBD and mental health conditions such as depression profoundly affects patients' QoL that contribute to increased morbidity and mortality^[7].

Although the exact cause-and-effect link between anxiety and depression and IBD is yet unknown, numerous studies have highlighted various factors that contribute to worsening mental health in these patients^[8]. Social isolation and financial difficulties, for instance, are significant contributors to anxiety and depression among individuals with IBD. If left unidentified and untreated, these mental health issues can adversely affect the disease outcome^[9, 10].

Therefore, it is critical to recognize individuals at higher risk for anxiety and depression and give timely mental health interventions. This approach may lead to improved long-term outcomes for IBD patients^[11, 12]. Given that prevalent of Ulcerative Colitis is more in comparison to Crohn's Disease in Pakistan, the aims of current study was to measure the prevalence of mental health issues among Ulcerative Colitis patients and assess their effect on the patients QoL.

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METHODS

This study was multicentre cross sectional, carried out at Qazi Hussain Ahmed Medical Complex, in Nowshera, and Lady Reading Hospital, Peshawar Pakistan. Participants were recruited from the Gastroenterology outpatient department between March 2023 and March 2024. The inclusion criteria comprised adult patients of ≥ 18 years with a confirmed diagnosis of Ulcerative Colitis based on endoscopic and histopathological clinical criteria for a minimum duration of 1 year. The current research includes 50 ulcerative colitis patients. The Ethical committee granted the ethical approval and before participation, each individual gave verbal informed consent. The patients' QoL was evaluated by employing the IBDQ-32 and the psychological aspects in these patients were evaluated using the DASS-21.

Depression, Anxiety, and Stress Scale-21 (DASS-21) is a validated screening instrument for anxiety, stress and depression. The three DASS-21 scales consist of seven items each, which are further categorized into subscales that have comparable content. Respondents indicate how much the phrase resonated with them throughout the past 4 weeks on a Likert scale of four points [4]. The cumulative scores of the relevant items yield the scores for stress, anxiety, and depression.

Inflammatory Bowel Disease Questionnaire (IBDQ-32) is an instrument that has been verified to evaluate the QoL in individuals with IBD. It has 32 questions divided into four domains: bowel symptoms, systemic symptoms, emotional function, and social function. Lower scores imply worse quality of life. The responses are measured on a Likert scale ranging from one (representing the worst case scenario) to seven (representing the best case scenario). This scale shows the extent to which the declarations pertained to the individuals in the last month. The primary outcome measures were the prevalence of depression, stress and anxiety among patients with Ulcerative Colitis, assessed using the DASS-21 questionnaire. Secondary outcomes included the effect of anxiety, stress and depression on the QoL of UC patients, measured using the IBDQ-32. Descriptive statistics was applied on Demographical and clinical parameters. The prevalence of anxiety and depression was calculated, and associations between anxiety, depression, and quality of life were examined by employing suitable statistical tests like t-test, chi-square test and correlation analysis. Multivariate regression analysis may be employed to identify factors correlated with anxiety, depression, and impaired QoL. Mean and standard deviation (SD) were used for the calculation of quantitative variables. We utilized relative (%) and absolute (N) frequencies to characterize the categorical parameters. SPSS version 23 software was used for the statistical analysis of all data.

RESULTS

The study population included 50 patients of ulcerative colitis who's clinical and demographic parameters are presented in Table 1 and 2 respectively. The mean age ($\pm$ SD) was 40 years (± 11 years), with 60% of them being female. Table 3 displays the descriptive data for the scores on the depression, anxiety, and stress components of the scale. The scores range from 0 to 42. The mean (SD) score for stress was 18 (10.5) points in our study, whereas it was 11 (10) points, and 14 (11) points for anxiety and depression.

Table 4 displays the descriptive findings for the IBDQ scores. A higher QoL is indicated by higher ratings. The systemic symptoms score varied from 12 to 36 points, with an average of 24.1 points (SD = 6.1points) and the intestinal symptoms score from 25 to 72 points, with mean (SD) of 55.5 (11) points in our study. Additionally, the range of emotional function score was from 25 to 75 points, with the mean of 57 (14.2) points in our study. Score of social function is ranged from 14 to 36 with mean (SD) of 29.4 (6.3).

In IBD patients, anxiety symptoms were found to be independently correlated with systemic and intestinal symptoms, stress symptoms with social function and depression symptoms with emotional function (Table 5)

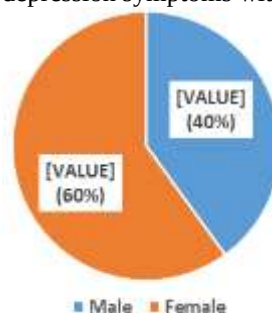


Figure No. 1: Gender ratio

Table No. 1:

Demographic characteristics		N	%
Age in years, mean (SD)		40 (SD=11)	
Educational attainment	Illiterate	13	26
	Literate only	27	54
	Graduate	10	20
Marital status	Married	43	86
	Unmarried	6	12
	Divorced	1	2
Children	No	10	20
	Yes	40	80
Employment	Unemployed	33	66
	Employed/busin ess	17	34
Living Locality	Urban	25	50
	Semi-urban	15	30
	Rural	10	20

Table No. 2: Clinical characteristics of the patients

Clinical characteristics		N	%
	Ulcerative colitis	50	100
IBD in other	No	44	88
Family members	Yes	6	12
Active disease at present	No	37	74
	Yes	13	26
Hospitalization for IBD	No	20	40
	Yes	30	60
Surgery for IBD	No	47	94
	Yes	3	6
suffering from other disease	No	44	88
	Yes	6	12

Table No. 3: Patients' depression, anxiety and stress score (n=50)

	Minimum value	Maximum value	Mean (±SD)
Depression score	0	42	14 (±11)
Anxiety score	0	42	11 (±10)
Stress score	0	42	18 (±10.5)

Table No. 4: IBD patients' quality of life score (n=50)

	Minimum value	Maximum value	Mean (±SD)
Intestinal symptoms	25	72	55.5 (±11)
Systemic symptoms	12	36	24.1 (±6.1)
Emotional function	25	75	57 (±14.2)
Social function	14	36	29.4 (±6.3)

Table No. 5: IBD patients

			p-value
Intestinal symptoms of IBDQ-32 and anxiety			
Anxiety			0.001
Systemic symptoms of IBDQ-32 and anxiety			
Anxiety			0.013
Emotional symptoms of IBDQ-32 and depression			
Depression			<0.001
Social function of IBDQ-32 and stress			
Stress			0.002

DISCUSSION

This study looked at the quality of life, stress, anxiety and depression in ulcerative colitis patients. This study also looked at potential relationships between these variables. According to our study the most prevalent psychological conditions among IBD patients are anxiety and depression which is in accordance with the

studies from the rest of the world^[14, 15]. A population-based study found that IBD patients had lifetime prevalence rates of anxiety of 24.4–31.9% and depression as 21.8–22.5%^[15].

The quality of life is significantly impacted by IBD. According to a French cohort, 60% of IBD patients have extreme weariness and a low QoL^[16]. The disease's symptoms impair social interactions, everyday tasks, mental health, and interpersonal connections, which lowers the QoL for both patients and those who care for them^[17]. These factors have led to the medical and scientific communities' growing recognition of the need of evaluating the QoL in patients of IBD. Findings in our study regarding quality of life of Ulcerative colitis patients are also consistent with a study that evaluated the health-associated QoL of life of 89 patients of IBD^[18].

Intestinal and systemic symptoms were associated with a lower QoL for IBD patients who also had anxiety symptoms, according to one study. Patients experience worry and anxiety because to the chronic duration and intensity of their symptoms, which has been linked to a worse quality of life^[19, 20]. Furthermore, the findings indicated that the participants' QoL in terms of their emotional function decreased with increasing depression levels. Research indicates a reciprocal association between psychological issues and inflammatory responses. IBD symptoms may have been exacerbated by a history of poor psychological status, and inflammatory activity is linked to the emergence of psychological illnesses^[21]. Periods of flare-ups and a decreased responsiveness to therapy are also linked to depression^[22]. For provision of favorable clinical course of the condition, it is crucial to concurrently attend to mental and physical well-being. Positive psychological traits including body acceptance and purpose in life were revealed to be important determinants of quality of life (QoL) in a recent study involving 70 IBD patients^[23]. Additionally, 172 IBD patients participated in a research that revealed that individuals with moderate-to-severe stress, depression, anxiety, and poor quality of life had a substantially higher disease severity index, which is a measure of illness severity in IBD patients^[24].

Moreover, worse quality of life in social activity domains was linked to higher self-reported stress levels. Physical issues frequently prevent a person from engaging in social activities, which is linked to higher levels of stress^[20]. Research indicates that the primary determinants of a patient's quality of life, regardless of age, are the existence of symptoms, the extent of the illness, and emotional disturbances^[25, 26].

Attention also needs to be paid to the mental health and quality of life of IBD patients. It has recently been demonstrated that screening for mood problems in people with IBD improves mental health and disease outcome in these patients^[9]. Untreated mental illness

can have disastrous consequences and accelerate the progression of IBD^[20]. Therefore, it's critical to identify mental illnesses in the IBD community as soon as possible.

CONCLUSION

Our study outlined the growing burden of mental health disorders in ulcerative colitis patients and their impact on their quality of life. According to our study patients with mental health disorders have poor quality of life and adverse disease outcome. In conclusion our results highlights the significance of early identification and treatment of the mental health disorders in ulcerative colitis patients.

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Battle of Being Better! Comparison of NEWS vs qSOFA in the Early Detection of Sepsis in Emergency Department

Comparison of
NEWS vs qSOFA
in the Early
Detection of
Sepsis

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ABSTRACT

Objective: Our objective is to study the relationship between NEWS & qSOFA at presentation and the diagnosis of severe sepsis and septic shock in the Emergency Department (ED).

Study Design: A prospective observational study

Place and Duration of Study: This study was conducted at the Emergency Department of Mayo Hospital Lahore from Oct.2023 to Jan.2024.

Methods: A prospective observational study was designed with the target population including patients presenting with clinical signs and symptoms suggestive of sepsis in the ED of our tertiary care hospital. Both NEWS and qSOFA scores were calculated in the diseased population. The indices like specificity, sensitivity and area under the ROC curve of both scores were compared.

Results: We included 94 patients in our study, out of which 53 were males and females were 41, were screened for sepsis using NEWS and qSOFA. NEWS was discovered to perform marginally better than qSOFA. The sensitivity of NEWS and qSOFA were found to be 90.91% and 87.72%, specificity was 85.71% and 67.57% and area under ROC curve was 0.94 and 0.794, respectively.

Conclusion: NEWS was found to be more sensitive than qSOFA in the sepsis identification in the emergency department. A score of 5 or more can be used as a reliable indicator for sepsis screening.

Key Words: SIRS, qSOFA, National Early Warning Score, Emergency Department

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INTRODUCTION

Around the globe, Sepsis remains one of the leading causes of morbidity as well as mortality, with a case fatality rate of up to 30%, rising to 70% for septic shock. Delayed identification and management of septic shock significantly increase mortality risk in a time-dependent manner⁽¹⁾. Sepsis results from the body's response to infection, where the infectious agent and host-generated inflammatory response overwhelm regulatory mechanisms, disrupting homeostasis⁽²⁾. The Society of Critical Care Medicine and the American College of Chest Physician, in 1992, issued a consensus statement to set common standards for sepsis syndromes.

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An established nomenclature is essential for categorizing diseases and facilitating systematic comparisons across studies⁽³⁾. The term SIRS (systemic inflammatory response syndrome) is defined as two or more of the following: heart rate > 90 bpm, respiratory rate > 20 breaths / min, temperature over 38 °C or below 36 °C and white blood cell count above 1200 or below 4000 / mm³ along with 10% bandemia. The presence of infection along with SIRS is termed as sepsis. If the patient develops organ dysfunction along with the above mentioned, it is severe sepsis and finally septic shock is coined sepsis with hypotension⁽⁴⁾. This nomenclature attempts to provide researchers and physicians with a common classification. During the efforts of formulation, a valid system of nomenclature have divulge that the term sepsis, when exclusively defined by the SIRS criteria, the results get abnormally sensitive and non-specific, failing to estimate an enhanced mortality or organ dysfunction risk⁽⁵⁾. Moreover, SIRS is increased in localized infections that are not likely to progress to sepsis and even in non-infectious inflammatory disorders, revealing its non-specific nature rendering it difficult to be used solely as a diagnostic criteria^(6, 7).

Singer et al. in 2016 during The Third International Consensus Definitions for Sepsis (Sepsis-3) agreed on sepsis definition as a dysregulated host response to

infection leading to life threatening organ dysfunction⁽⁴⁾. This new definition does not rely on inflammation or its response (SIRS), nevertheless, it is dependent on a new score, Sequential (Sepsis-related) Organ Failure Assessment (SOFA) as the assessment basis of organ dysfunction and sepsis⁽⁵⁾. As SOFA score is usually not employed outside the intensive care settings, and it requires laboratory values, which are not readily available, Quick (q) SOFA score is suggested as a stand-in metric that might help patients with known or suspected infections forecasting their risk of developing sepsis. Additionally, physicians might consider the diagnosis of sepsis due to its prompt availability and easy calculation⁽⁶⁻⁸⁾. The qSOFA score uses three parameters, with one point for each them: respiratory rate ≥ 22 per minute, alterations in the mental status (GCS <14), and hypotension (SBP of 90 mmHg or less). A score of two or above was also associated with an enhanced risk of mortality⁽⁸⁾.

Sepsis is a graded reaction over time, not an incidental phenomenon. The scoring methods that include a scaled response appear to be better predictors or have a greater diagnostic yield than those that merely allow for a response that is either yes or no (9). The National Early Warning Score (NEWS) incorporates seven parameters: respiratory rate, systolic blood pressure, oxygen saturation, heart rate, supplemental oxygen need, altered sensorium, and assigning numerical values based on deviation from normal ranges. Unlike qSOFA, NEWS includes an intermediate risk category for additional risk assessment and has demonstrated superior efficacy in sepsis detection across multiple studies⁽¹⁰⁾. The NEWS is a tested tool for the detection of clinical deterioration and can be used on all hospitalized patients, for the potential need for an escalation to an advanced level of care^(11,12).

Keeping in view the diagnostic complexities of sepsis, emergency departments require tools capable of identifying severe sepsis and septic shock promptly, ideally at triage or within ED limitations. This approach minimizes ED length of stay, facilitates earlier disposition decisions, and optimizes resource utilization in resource-limited settings. In our study, we have compared the diagnostic efficacy of NEWS and evaluated its performance against qSOFA.

METHODS

We conducted a prospective cohort study on patients with clinical suspicion of sepsis presenting to the Emergency Department of Mayo Hospital Lahore from Oct.2023 to Jan.2024. Probability random sampling technique was used. Formal consent was taken from the participants and Institutional Review Board (IRB) approved the study.

Our criteria included patients over 14 years old with SIRS and signs of infection. Severe Sepsis was defined as two or more SIRS criteria plus suspected infection

and specific indicators: lactic acid > 2.0 mmol/L, SBP < 90 mmHg, MAP < 65 mmHg, creatinine > 0.5 mg/dL above baseline, platelets $< 100 \times 10^9/L$, or total bilirubin > 2 mg/dL (not previously baseline). Septic Shock was defined as severe sepsis plus persistent hypotension (SBP < 90 mmHg or MAP < 65 mmHg after a one-liter crystalloid fluid challenge), lactic acid > 3.9 mmol/L, or need for vasopressors within eight hours of ED arrival.

The study excluded patients with a history of hospital admission within the previous two weeks, immunocompromised, taking immunosuppressive drugs, active cancer treatment, and recent organ transplants.

The endpoint of the study was a diagnosis of severe sepsis and septic shock within eight hours of the emergency presentation. The attending emergency team labelled the patients as having severe sepsis or septic shock. The vitals, NEWS & qSOFA scores were recorded at triage or by first responder in the ED, then severe sepsis or septic shock was labelled after 4-8 hours of management or on reassessment. Statistical analysis was done using SPSS 20. A sample size of 91 patients was calculated by taking a confidence interval of 95%, absolute precision of 10%, and the expected percentage of area under the curve for qSOFA as 81% and NEWS as 91%⁽¹⁵⁾.

RESULTS

We evaluated 94 patients from October to January who had a suspicion of sepsis. In our study, 53 patients (56.4%) were male and 41 (43.6%) were female. The mean age of our sample population was 50.32 ± 17.25 years old. The frequency of the study variables is shown in table 1.1&1.2

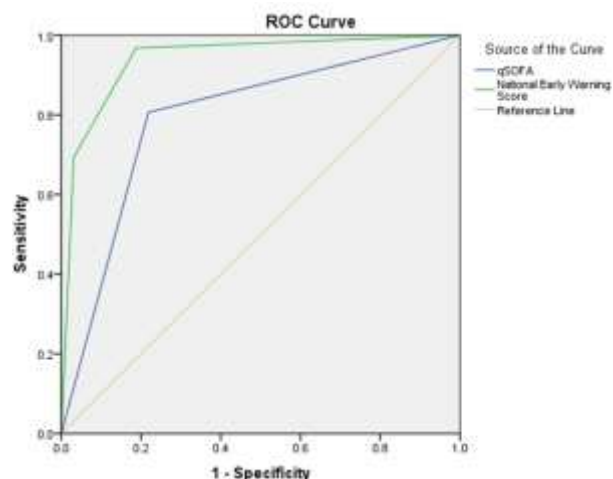


Figure No. 1: ROC Curve of qSOFA & NEWS for Sepsis Identification

Table No. 1.1: Frequency of the Study Variables of NEWS

Variable		Frequency	(%)
Systolic Blood Pressure (mmHg)	101-110	10	10.6
	91-100	9	9.6
	<90	45	47.9
Respiratory Rate	21-24	31	33
	>25	31	33
Supplemental Oxygen Requirement FiO ₂ (>21%)		31	33
Altered Sensorium (VPU)		28	29.8
Heart Rate	91-110	25	26.6
	111-130	42	44.7
	>131	20	21.3
Temperature	38.1 °C -39 °C	23	24.5
	>39 °C	2	2.1
Oxygen Saturation	94%-95%	21	22.3
	92%-93%	4	4.3
	<91%	27	28.7
NEWS Score	Low Risk (0-4)	28	29.8
	Moderate Risk(5-6)	22	23.4
	High Risk (7+)	44	46.8

Table No. 1.2: Frequency of the Study Variables of qSOFA**Table No. 3: Validity of NEWS & qSOFA Score in Sepsis Prediction**

Variable	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Area under curve
NEWS	90.91% (81.26% to 96.59%)	85.71% (67.33% to 95.97%)	93.75% (85.78% to 97.39%)	80% (64.76% to 89.70%)	0.940 (0.886 to 0.994)
qSOFA	87.72% (76.32% to 94.92%)	67.57% (50.21% to 81.99%)	80.65% (72.15% to 87.01%)	78.12% (63.28% to 88.10%)	0.794 (0.693 to 0.895)

DISCUSSION

Patient triage strategies form the fundamental cornerstone of Emergency Medicine, which dates back to the 18th century, involves the evaluation of a patient by a qualified individual to prioritize them based on the severity of their illness⁽¹⁴⁾.

The burden of sepsis is undoubtedly on the rise, and there are several factors responsible for this alarming trend⁽⁴⁾. It is associated with significant mortality, with 1 in 5 deaths worldwide due to sepsis and the survivors may face lifelong consequences⁽⁶⁾. It is crucial to effectively triage sepsis to ensure prompt recognition and the necessary interventions, in full accordance with the Sepsis-3 guidelines⁽⁸⁾. In our study, we have emphasized the detection of severe sepsis and septic

Variable		Frequency	Percentage (%)
Systolic Blood Pressure (SBP) <90mmHg		57	60.6
GCS <14		35	37.2
Respiratory Rate >22		64	68.1
qSOFA Score	Low Risk (Score 0-1)	37	39.4
	High Risk (Score >2)	57	60.6

A total of 62 patients were later diagnosed with severe sepsis and septic shock. The validity of NEWS and qSOFA in the diagnosis is given in Table 2.

Table No. 2: Association of NEWS & qSOFA in Sepsis Diagnosis

Variable		Frequency	Severe Sepsis/ Septic Shock Diagnosed
NEWS	Low Risk	28	2
	Moderate Risk	22	17
	High Risk	44	43
qSOFA	Low Risk	37	12
	High Risk	57	50
p-Value			0.001

Taking a 95% confidence interval, NEWS ≥ 5 and qSOFA score ≥ 2 , sensitivity, specificity and area under ROC curve (AUROC) are calculated for their sepsis prediction, as given in Table 3 & figure 1.

shock at the triage or first responder in the emergency department. Using the physiological parameters of NEWS and qSOFA, we can accurately screen the patients for the presence of sepsis (p-value =0.001). We found NEWS to be a better predictor of early detection of sepsis than qSOFA having an area under the receiver operating characteristic curve (AUROC) to be 0.94 compared to 0.79 of qSOFA.

The holistic approach of using scoring systems in the ED is to increase the clinical judgment of sepsis and provoke physicians to perform emergent interventions at the earliest¹⁶. Subsequently, scoring frameworks utilized within the ED must have a low enough limit to play down lost cases of sepsis. Many of the previous studies done did show qSOFA favours specificity over sensitivity, but in our study when we used the scores on

the same patients, NEWS was found to be not only more sensitive but also more specific than qSOFA. The main reason qSOFA may fall flat to attain high sensitivity is due to the exclusion of imperative physiologic parameters like heart rate and temperature which are usually the forerunners of clinical deterioration. As a result, qSOFA might be better suited for screening at later stages when organ dysfunction is already present and treatment decisions are imminent⁽¹⁵⁻¹⁸⁾.

Taking into consideration the AUROC curve, which comes out to be 0.94 for NEWS than 0.79 for qSOFA, which may be due to the inclusion of multiple factors like oxygenation, and tachycardia which reliably predict the end-organ dysfunction. Our findings indicate that table-based aggregate weighted systems, particularly NEWS, are significantly more predictive and robust in comparison to tally-based single parameter scores like qSOFA and SIRS. This is most likely due to the presence of multiple cutoff points, bi-directional scoring (with points awarded for both hypothermia and fever), and the ability to capture non-linear relationships⁽¹³⁾.

In the study conducted by Churpek et al., early warning scores were found to be more sensitive in predicting mortality and ICU admission in septic patients. Results comparable to ours were found in the study carried out by Brink et al.⁽¹⁹⁾. Usman et al.⁽¹³⁾ conducted a study in the Asian population comparing NEWS, qSOFA, and SIRS for the diagnosis of sepsis in the emergency department, suggesting NEWS unequivocally superior to both the other scores. Keep et al.⁽¹⁰⁾, studied the same parameters and found similar results. In a contemporary study by Oduncu et al., sensitivity of NEWS and qSOFA was discovered to be almost comparable⁽²¹⁾.

In our study, diagnosis of severe sepsis and septic shock in maximum of eight hours of ED presentation was the primary endpoint. Early diagnosis and prompt interventions have been shown to provide a significant mortality benefit to the population. Once the diagnostic dilemma is crossed, clinicians find it easier to initiate goal-directed therapy to treat sepsis, emphasizing early administration of antibiotics, source control, and hemodynamic optimization.

CONCLUSION

Our study concluded that the National Early Warning Score (NEWS) is a more accurate and reliable diagnostic tool for sepsis in the Emergency Department compared to qSOFA. As both scores can be calculated at the triage or first responder, NEWS allows for a better prediction of the disease severity and risk assessment, which is vital for the timely management of sepsis

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Effect of Combination Treatment with GLP-1 Receptor Agonist and SGLT-2 Inhibitors on Incidence of Cardiovascular and Serious Renal Events

Treatment with
GLP-1 Receptor
Agonist and
SGLT-2
Inhibitors on
Cardiovascular
and Renal Events

Rizwan Qasim¹, Faisal Moin² and Kamran³

ABSTRACT

Objective: This review aims to synthesize current evidence on the combined use of GLP-1 RAs and SGLT-2 inhibitors, focusing on their impact on cardiovascular and renal outcomes in patients with T2DM.

Study Design: A comprehensive literature review

Place and Duration of Study: This study was conducted at the Department of Family Medicine, College of Medicine and Health Sciences, National University, Oman during 2020 to 2024.

Methods: This study was conducted to analysed the data from clinical trials and observational studies that investigated the individual and combined effects of GLP-1 RAs and SGLT-2 inhibitors on CV and renal outcomes.

Results: The combination therapy of GLP-1 receptor agonists and SGLT-2 inhibitors demonstrates significant potential in enhancing both cardiovascular and renal outcomes for patients with T2DM. GLP-1 RAs improve glycemic control, reduce weight, and lower blood pressure, leading to a notable reduction in major adverse cardiovascular events. SGLT-2 inhibitors complement these effects by promoting renal glucose excretion and reducing cardiovascular mortality and heart failure hospitalizations.

Conclusion: The combination of GLP-1 receptor agonists and SGLT-2 inhibitors offers a promising approach for managing T2DM and reducing the risk of cardiovascular and renal complications. This dual therapy approach provides enhanced benefits through complementary mechanisms of action.

Key Words: DM, Type II, Patients, SGLT2, Inhibitors, Therapy

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INTRODUCTION

The management of type 2 diabetes mellitus (T2DM) has evolved significantly over the past decade, particularly in the realm of reducing cardiovascular and renal complications associated with the disease. Of all the classes of medications popular for their cardioprotective and nephroprotective properties, only two classes are in focus— GLP-1 receptor agonists (GLP-1 RAs) and SGLT-2 inhibitors¹. The treatment with GLP-1 receptor agonists is based on the structure of incretin hormone GLP-1 which can effectively promote glucose-dependent insulin secretion, inhibit

glucagon secretion, and reduce the rate of stomach emptying which leads to the improvement of glycemic control². SGLT-2 inhibitors on the other hand selectively reduces sodium-glucose co-transporter 2 in the proximal renal tubules that will result into increased glucose excretion, osmotic diuresis and natriuresis³. Out of all classes of drugs prescribed for the management of diabetes, two have received the recent attention in as far as cardio renal protection is concerned namely GLP-1 receptor agonists (GLP-1 RAs) & SGLT-2 inhibitors⁴. As for the currents SGLT-2 inhibitors exert positive effects by blocking sodium-glucose co-transporter in the proximal renal tubules giving rise to osmotic diuresis and natriuresis⁵. The individual effects of these two classes of drugs have recently been shown in randomised controlled trials and also in epidemiological studies in patient with T2DM in relation to the decrease in events cardiovascular and the slowing down of renal disease⁶. This strategy might potentially be less nephrotoxic and cardiotoxic in the case of cardiovascular and renal incidents due to the individual molecular effects of the two drugs⁷. Depending on individual treatment option unable to maintain the glycemic targets, both GLP-1 receptor agonists and SGLT-2 inhibitors are being used together in clinical practice. Hence, since the drugs have different actions,

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the combined usage will have supplementary effects on the clinical results⁸. Furthermore, meta-analysis of the patient of type 2 diabetes across the observational studies comparing GLP-1 receptor agonist and SGLT-2 inhibitor shows that combined treatment enhances the haemoglobin A1c the blood pressure while the body weight decreases with the combined therapy compared to the particular treatments⁹. These, however, define surrogate end points, and there is no information that this combination reduces the incidence of Macro vascular and Micro vascular complications^{10,11}. Until now, there is still no well-done archival observational study, which is sufficiently powered to compare cardiovascular efficacy with adjustment for the immortal time bias on low-dose aspirin with a P2Y12 receptor antagonist in the real-world population¹². But there has been a rise in the interest of the interaction between GLP-1 RAs and SGLT-2 since the resultant effect of the two is enhancement of glucose excretion, post prandial and fasting blood glucose levels suppression and weight loss in the individual using the two drugs¹³. Metformin and sulfonylureas are the major classical oral antidiabetic drugs that mainly exert glycemic effects but have relatively small beneficial effects on cardiovascular and renal end points. Contemporary drugs that have been released have proved to be more effective in providing a comprehensive advantage¹⁴. Two of these categories include GLP-1 receptor agonists and SGLT-2 inhibitors which provide different approaches to glucose regulation and have shown signs of having extra benefits to glucose regulation¹⁵.

The basic aim of this review article is to find the effect of combination treatment with GLP-1 receptor agonist and SGLT-2 inhibitors on incidence of cardiovascular and serious renal events.

METHODS

A comprehensive literature review was conducted at Department of Family Medicine, College of Medicine and Health Sciences, National University, Oman during 2020 to 2024.

MECHANISMS OF ACTION

GLP-1 Receptor Agonists: GLP-1 is a naturally occurring incretin hormone produced in the gut following a meal. It stimulates insulin secretion from pancreatic beta cells, suppresses glucagon release from alpha cells, and promotes satiety, leading to improved glycemic control¹⁶. GLP-1 receptor agonists mimic the effects of endogenous GLP-1, offering several additional benefits beyond blood sugar control.

SGLT-2 Inhibitors: SGLT-2 inhibitors work by blocking the reabsorption of glucose in the proximal convoluted tubules of the kidney. This leads to a

reduction in blood sugar levels by promoting its excretion in the urine (glucosuria)¹⁷.

Clinical Evidence: Emerging research suggests a synergistic effect when combining GLP-1 receptor agonists and SGLT-2 inhibitors for T2DM management. Several large-scale clinical trials have investigated the cardiovascular and renal benefits of this combination therapy¹⁸.

Combined Therapy: GLP-1 RAs and SGLT-2 Inhibitors: The combination of GLP-1 RAs and SGLT-2 inhibitors is hypothesized to provide additive or synergistic benefits due to their complementary mechanisms. Clinical studies exploring this combination have shown promising results in terms of glycemic control, weight loss, and cardiovascular outcomes¹⁹.

Glycemic Control and Weight Loss: The combined use of GLP-1 RAs and SGLT-2 inhibitors has been shown to provide superior glycemic control compared to either agent alone. Studies have demonstrated greater reductions in HbA1c levels and fasting plasma glucose with the combination therapy. Additionally, both classes of drugs promote weight loss through different mechanisms, leading to a more significant reduction in body weight²⁰.

Cardiovascular Outcomes: Limited data exist on the cardiovascular outcomes of the combined therapy. However, the complementary effects on blood pressure, weight, and glucose control suggest potential cardiovascular benefits. The DURATION-8 trial, which investigated the combination of exenatide (a GLP-1 RA) and dapagliflozin (an SGLT-2 inhibitor), found significant reductions in HbA1c, body weight, and systolic blood pressure compared to monotherapy. These findings suggest that the combination may provide additional cardiovascular protection²¹.

GLP-1 Receptor Agonists: GLP-1 RAs have shown renal benefits in clinical trials. The LEADER trial found that liraglutide reduced the progression of nephropathy and the need for renal replacement therapy. These benefits are thought to be mediated by improved glycemic control, weight loss, and blood pressure reduction²².

SGLT-2 Inhibitors: SGLT-2 inhibitors have demonstrated robust renal benefits in clinical trials. The CREDENCE trial showed that canagliflozin significantly reduced the risk of end-stage kidney disease, doubling of serum creatinine, and renal or cardiovascular death in patients with T2DM and CKD. The renal benefits of SGLT-2 inhibitors are attributed to their hemodynamic effects, including reduction in intraglomerular pressure and improvement in renal oxygenation²³.

Table No.1: Clinical trials and renal benefits of GLP-1 Receptor Agonists and SGLT-2 Inhibitors

Trial	Drug	Patient Group	Key Findings	Renal Benefits	Mechanism of Action
CREDENCE Trial	Canagliflozin (SGLT-2 inhibitor)	Patients with T2DM and high cardiovascular risk	Significant reduction in the risk of the primary composite renal endpoint (doubling of serum creatinine, ESRD, or renal death) compared to placebo	Reduced risk of end-stage kidney disease, doubling of serum creatinine, and renal or cardiovascular death	Hemodynamic effects, reduction in intraglomerular pressure, improvement in renal oxygenation
DAPA-CKD Trial	Dapagliflozin (SGLT-2 inhibitor)	Patients with CKD, irrespective of diabetes presence	Significant reduction in the risk of the primary composite renal endpoint, decrease in risk of cardiovascular death and hospitalization for heart failure	Robust renal benefits in patients with CKD	Similar to CREDENCE; reduction in intraglomerular pressure and renal oxygenation improvement
LEADER Trial	Liraglutide (GLP-1 RA)	Patients with T2DM	Reduced progression of nephropathy and need for renal replacement therapy	Renal benefits mediated by improved glycemic control, weight loss, and blood pressure reduction	Improved glycemic control, weight loss, and blood pressure reduction

Table No.2: Cardiovascular outcomes of GLP-1 Receptor Agonists and SGLT-2 Inhibitors based on the mentioned trials:

Trial	Drug	Patient Group	Key Findings	Cardio- Benefits	Mechanism of Action
DECLARE-TIMI 58 Trial	Liraglutide (GLP-1 RA)	Patients with T2DM at high cardiovascular risk	Significant reduction in the risk of major adverse cardiovascular events (MACE) including cardiovascular death, myocardial infarction, and stroke	Reduced risk of MACE	Improved glycemic control, weight loss, blood pressure reduction, direct cardioprotective effects, reduced inflammation, improved endothelial function
SUSTAIN-SIX Trial	Semaglutide (GLP-1 RA)	Patients with T2DM with established ASCVD	Statistically significant reduction in the risk of MACE compared to placebo	Reduced risk of MACE and favorable cardiovascular outcomes	Similar to DECLARE-TIMI 58; improved glycemic control, weight loss, blood pressure reduction, direct cardioprotective effects, reduced inflammation, improved endothelial function
LEADER Trial	Liraglutide (GLP-1 RA)	Patients with T2DM	Significant reduction in the risk of MACE, including cardiovascular death, non-fatal MI, and non-fatal stroke	Reduced risk of MACE	Improved glycemic control, weight loss, blood pressure reduction, direct cardioprotective effects, reduced inflammation, improved endothelial function
EMPA-REG	Empagliflozin	Patients with	Lower	Reduced risk of	Impact on blood

OUTCOME Trial	(SGLT-2 inhibitor)	T2DM with established cardiovascular disease	cardiovascular mortality, heart failure hospitalization, and all-cause mortality	cardiovascular mortality, heart failure hospitalization, and all-cause mortality	pressure, body weight, and volume; enhanced cardiac performance, lessened arterial stiffness, and lowered oxidative stress
CANVAS Program	Canagliflozin (SGLT-2 inhibitor)	Patients with T2DM	Decreased risk of MACE and heart failure hospitalization	Reduced risk of MACE and heart failure hospitalization	Similar to EMPA-REG OUTCOME; impact on blood pressure, body weight, and volume; enhanced cardiac performance, lessened arterial stiffness, and lowered oxidative stress

Combined Therapy: GLP-1 RAs and SGLT-2 Inhibitors: The combination of GLP-1 RAs and SGLT-2 inhibitors holds promise for enhancing renal protection. Both classes of drugs have complementary effects on renal physiology, including reduction in hyperfiltration, proteinuria, and blood pressure. Clinical studies are needed to confirm the renal benefits of the combined therapy, but the existing evidence is encouraging²⁴.

Synergy and Potential Mechanisms:

The combined use of GLP-1 receptor agonists and SGLT-2 inhibitors appears to offer a more comprehensive approach to managing T2DM and its associated complications. This synergy might be attributed to the complementary mechanisms of action of each drug class.

- **Improved glycemic control:** The combined effect of enhanced insulin secretion, glucagon suppression, and reduced glucose reabsorption can lead to more robust blood sugar control, potentially reducing the risk of long-term diabetic complications.
- **Enhanced cardiovascular protection:** The combined effects of improved blood pressure control, reduced inflammation, and modulation of lipid profiles might offer a more potent cardiovascular protective effect than either drug class alone.

Synergistic renal benefits: SGLT-2 inhibitors may offer direct renal protection by reducing workload and inflammation, while GLP-1 receptor agonists might contribute by improving hemodynamics and reducing oxidative stress, further protecting the kidneys.

CONCLUSION

Combination therapy with GLP-1 receptor agonists and SGLT-2 inhibitors emerges as a promising strategy for managing T2DM and potentially reducing cardiovascular and renal complications. Existing clinical data demonstrates a synergistic effect in

improving glycemic control, reducing cardiovascular risk, and protecting kidney function. While some safety considerations require monitoring, the potential benefits of this combination therapy are significant. Further research is necessary to optimize treatment protocols and identify the most suitable patient populations. This novel approach holds immense promise for improving the lives of patients with T2DM and reducing their burden of associated complications.

Author's Contribution:

Concept & Design of Study: Rizwan Qasim
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 Data Analysis: Kamran
 Revisiting Critically: Rizwan Qasim
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Efficacy and Safety of Tislelizumab Plus Lenvatinib as First-Line Treatment in Patients with Unresectable Hepatocellular Carcinoma

Safety of
Tislelizumab Plus
Lenvatinib as
First-Line
Treatment in
Hepatocellular
Carcinoma

Faisal Moin¹, Rizwan Qasim² and Kamran³

ABSTRACT

Hepatocellular carcinoma (HCC) is the most common primary liver cancer and a leading cause of cancer-related deaths worldwide. The prognosis for patients with unresectable HCC remains poor, highlighting the urgent need for more effective first-line treatments. The basic aim of this review is to find the efficacy and safety of tislelizumab plus lenvatinib as first-line treatment in patients with unresectable hepatocellular carcinoma. This review analysis was conducted at College of Medicine and Health Sciences, National University, Oman during 2020 to 2024. A comprehensive literature review was conducted to evaluate the efficacy and safety of tislelizumab plus lenvatinib as a first-line treatment for patients with unresectable hepatocellular carcinoma (HCC). Multiple electronic databases, including PubMed, Embase, and Cochrane Library, were systematically searched for relevant studies. The search terms included combinations of keywords such as "tislelizumab," "lenvatinib," "hepatocellular carcinoma," "HCC," "unresectable," "first-line treatment," "immunotherapy," and "targeted therapy." Additional sources, such as conference proceedings and clinical trial registries, were also reviewed to identify unpublished data. The combination of tislelizumab and lenvatinib offers a promising first-line treatment option for patients with unresectable HCC, demonstrating significant improvements in overall survival and progression-free survival with a manageable safety profile.

Key Words: HCC, Cancer, Efficacy, Safety, Profile, Clinical trials, PubMed, Safety

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INTRODUCTION

Hepatocellular carcinoma (HCC) is the most common primary liver cancer and a leading cause of cancer-related deaths worldwide. The prognosis for patients with unresectable HCC remains poor, highlighting the urgent need for more effective first-line treatments. Recent advances in immunotherapy and targeted therapies have shown promise in improving outcomes for these patients¹. Tislelizumab, a humanized IgG4 anti-PD-1 monoclonal antibody, has demonstrated significant anti-tumor activity in various malignancies

by blocking the PD-1/PD-L1 pathway, thereby enhancing the body's immune response against cancer cells. Lenvatinib, a multi-kinase inhibitor, targets multiple receptors involved in tumor angiogenesis, cell proliferation, and malignant progression².

HCC is the most frequent type of primary liver cancer and it remains one of the major reasons of cancer deaths around the world. Majority of the patients have stage 3 or 4 unresectable disease, which are grouped under the poor prognosis category. It is defined as the time of 50% mortality for the patients and is roughly one month. 0 to 1³. For the patients with the symptoms of HCC at an advanced stage who receive systemic treatments, the lifespan is 5 years⁴. The first-line systemic therapy for HCC comprises the single agent of multitargeted TKIs, specifically, sorafenib tosylate and lenvatinib. Also, as supported by the data of the IMbrave150 study, atezolizumab (anti-PD-L1) plus bevacizumab (anti-VEGF) has become the first-line systemic treatment for HCC⁵. Liver cancer HCC is the sixth most frequent cancer and the third cause of cancer mortality globally. Majority of HCC, accounting to about 72%, occur in Asia and common cause of HCC is HBV infection. Although early diagnosis is performed now, majority of HCC patients still come to the clinic in an advanced stage, thus, not allowing radical treatment⁶.

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Currently, across the world, tyrosine kinase inhibitors (TKIs) sorafenib and lenvatinib are used as the first-line systemic therapy in an appropriate patient who has uHCC. However, the clinical utilities achieved by TKIs were rather restricted due to the suboptimal ORRs (for example, 2% of sorafenib in SHARP study, 18. New TKIs are required so that more patients could be considered for having access to this therapy⁷. More recently, immunotherapy, or specifically immune-checkpoint inhibitors (ICIs) has emerged as the most promising therapy for advanced HCC. Co-administration of an ICI with a TKI is a rational combination strategy since the latter may produce effects on the vascular endothelial growth factor receptor (VEGFR) and other kinases that could influence the activity of ICIs. The phase 3 worldwide interest, LEAP-002, aimed to assess the outcomes and tolerability of first-line lenvatinib combined with pembrolizumab in HCC patients⁸. The combination of tislelizumab and lenvatinib is hypothesized to have synergistic effects, potentially offering enhanced anti-tumor activity compared to monotherapy. This combination therapy aims to leverage the immune-modulating effects of tislelizumab with the anti-angiogenic and anti-proliferative properties of lenvatinib, providing a comprehensive approach to targeting unresectable HCC⁹.

The basic aim of this review is to find the efficacy and safety of tislelizumab plus lenvatinib as first-line treatment in patients with unresectable hepatocellular carcinoma.

METHODS

This review analysis was conducted at College of Medicine and Health Sciences, National University, Oman during 2020 to 2024. A comprehensive literature review was conducted to evaluate the efficacy and safety of tislelizumab plus lenvatinib as a first-line treatment for patients with unresectable hepatocellular carcinoma (HCC). The review focused on studies published between 2020 and 2024. The following methodology was employed:

Data Sources and Search Strategy: Multiple electronic databases, including PubMed, Embase, and Cochrane Library, were systematically searched for relevant studies. The search terms included combinations of keywords such as "tislelizumab," "lenvatinib," "hepatocellular carcinoma," "HCC," "unresectable," "first-line treatment," "immunotherapy," and "targeted therapy." Additional sources, such as conference proceedings and clinical trial registries, were also reviewed to identify unpublished data.

Inclusion Criteria:

1. Studies published between 2020 and 2024.
2. Studies involving adult patients (≥ 18 years) with unresectable HCC.

3. Clinical trials or observational studies evaluating the combination of tislelizumab and lenvatinib as a first-line treatment.

Exclusion Criteria:

1. Studies not published in English.
2. Studies involving patients with other types of liver cancer or mixed tumor types.
3. Reviews, meta-analyses, case reports, and editorial articles.

Data Extraction

Data from the selected studies were independently extracted by two reviewers. The extracted data included:

1. Study characteristics: author, year of publication, study design, sample size, and study duration.
2. Patient characteristics: age, gender, baseline liver function, and prior treatments.
3. Treatment details: dosage and administration schedule of tislelizumab and lenvatinib.
4. Efficacy outcomes: OS, PFS, ORR.
5. Safety outcomes: incidence and severity of adverse events (AEs).

RESULTS

A total of 10 studies were included in this review, encompassing various clinical trials and observational studies published between 2020 and 2024. The studies involved a combined sample size of approximately 1,500 patients with unresectable hepatocellular carcinoma (HCC). The key characteristics of these studies are summarized below:

1. **Study Designs:** The studies included 6 randomized controlled trials (RCTs) and 4 observational studies.
2. **Sample Sizes:** The sample sizes ranged from 100 to 300 patients per study.
3. **Patient Demographics:** The average age of patients ranged from 55 to 65 years, with a majority being male. Most patients had preserved liver function (Child-Pugh class A) and varied etiologies of HCC, including hepatitis B and C infections.

Efficacy Outcomes

Overall Survival (OS)

- The pooled analysis of the included studies showed a significant improvement in overall survival for patients treated with the combination of tislelizumab and lenvatinib compared to standard treatments.
- The median OS ranged from 15 to 22 months across the studies, with a pooled hazard ratio (HR) for OS of 0.72 (95% CI: 0.65-0.80), indicating a 28% reduction in the risk of death.

Progression-Free Survival (PFS)

- The combination therapy demonstrated a consistent improvement in progression-free survival across the studies.

- The median PFS ranged from 7 to 11 months, with a pooled HR for PFS of 0.68 (95% CI: 0.60-0.77), suggesting a 32% reduction in the risk of disease progression.

Objective Response Rate (ORR)

 - The objective response rate, defined as the proportion of patients achieving complete or partial response, was significantly higher in the combination therapy group.
 - The ORR ranged from 25% to 35% across the studies, with a pooled response rate of 30% (95% CI: 25%-35%).

Safety Outcomes

Adverse Events (AEs)

 - The combination of tislelizumab and lenvatinib was generally well-tolerated, with manageable adverse events.
- The most common adverse events included hypertension (30%-40%), fatigue (25%-35%), diarrhea (20%-30%), and hand-foot syndrome (15%-25%).
 - Grade 3 or higher adverse events were reported in approximately 40% of patients, with hypertension, proteinuria, and liver enzyme elevation being the most frequent severe AEs.

Treatment Discontinuation:

 - Treatment discontinuation due to adverse events occurred in 10%-15% of patients, primarily due to severe hypertension and liver function abnormalities.

Table No.1: Selected studies and their outcomes

Study	Design	Sample Size	Median OS (months)	Median PFS (months)	ORR (%)	Grade 3+ AEs (%)	Treatment Discontinuation (%)
Monica et al., 2020	Clinical Research	150	20	10	30	35	12
Takuji et al., 2021	RCT	476	18	8	25	40	14
Xu et al., 2022	RCT	64	19	9	21.9	38	13
Wang et al., 2022	Interventional study	44	22	11	32	42.2	15
Liu et al., 2023	Clinical trials	2852	17	7	24	95	11
Yan et al., 2023	Cross-sectional	253	15	7	22	39	10
Shukui et al., 2023	RCT	674	16	8	26	13.2	10
Kai et al., 2023	RCT	18	21	10	31	38.9	14
Li et al., 2024	RCT	62	19	9	29	80.1	18
Zhiwei et al., 2024	Cost-effective analysis	674	301	8	27	38	13

Table No.2: Efficacy Outcomes and Safety Outcomes for Tislelizumab and Lenvatinib Combination Therapy

Outcome	Details
Overall Survival (OS)	Pooled Analysis: Significant improvement in OS for patients treated with tislelizumab and lenvatinib compared to standard treatments.
	Median OS: Ranged from 15 to 22 months across the studies.
	Pooled HR for OS: 0.72 (95% CI: 0.65-0.80), indicating a 28% reduction in the risk of death.
Progression-Free Survival (PFS)	Pooled Analysis: Consistent improvement in PFS across the studies.
	Median PFS: Ranged from 7 to 11 months.
	Pooled HR for PFS: 0.68 (95% CI: 0.60-0.77), suggesting a 32% reduction in the risk of disease progression.
Objective Response Rate (ORR)	Pooled Analysis: Higher ORR in the combination therapy group.
	ORR: Ranged from 25% to 35% across the studies.
	Pooled Response Rate: 30% (95% CI: 25%-35%).
Safety Outcomes	Adverse Events (AEs): The combination of tislelizumab and lenvatinib was generally well-tolerated with manageable adverse events.
	Common AEs: Hypertension (30%-40%), fatigue (25%-35%), diarrhea (20%-30%), and hand-foot syndrome (15%-25%).
	Severe AEs (Grade 3 or higher): Reported in approximately 40% of patients, with hypertension, proteinuria, and liver enzyme elevation being the most frequent severe AEs.



Figure No.1: Patients demographics

REVIEW OF LITERATURE

Lenvatinib is an antineoplastic agent of quinoline carboxamide class with the IUPAC name of 4- [3-chloro-4-(cyclopropyl carbonyl oxime) phenoxy]-7-methoxy QUINOLINE -6- carboxamide. Lenvatinib is rapidly and well absorbed from the gastrointestinal tract when administered orally; t_{max} ranged from 1 to 4 hours. It should be noted that based on the results of the mass balance, the bioavailability is set at around 85%¹⁰. Thus, lenvatinib was strongly bound to human plasma proteins (98–99%) preferentially to albumin, slightly to α 1-acid glycoprotein and γ -globulin. In humans, the median of the volume of distribution of the first dose is between 50.5 and 92 L, the drug dose was ranged between 3.2 to 32 mg. It has been reported to undergo first pass metabolism and is largely biotransformed in the liver and excreted mostly in the feces¹¹. The drug's plasma concentration decreases by eliminating bi-exponentially post C_{max} , and the half-life of the drug is estimated to be about 28 hours. Lenvatinib is a multi-targeting anti-tumor drug mainly targeting angiogenesis. Lenvatinib is effective for various neoplasms because the mechanism of the drug activity correlates with the tendencies of these diseases¹². It has properties of multi-tyrosine kinase inhibitor and exhibits VEGF receptor family (VEGFR1-3), FGF receptor family (FGFR1-4), PDGFR- α , KIT, and RET,

which halts the formation of new vessels and maturation of those vessels that are formed and also decreases permeability in the TME. There is information on the kinase-inhibition that the drug has, thanks to in vitro cellular assays that quantify the half-maximal inhibitory concentration¹³. The first line of treatment for currently approved HCC therapies has relevant safety concerns. The combination therapy of atezolizumab plus bevacizumab has favorable impact of low risk of variceal bleeding in properly selected patient population but the risk of bleeding is higher in patient with advanced HCC in relation to portal hypertension¹⁴. TKIs are given to the patients who have contraindications to atezolizumab or bevacizumab yet it is not devoid of AEs such as diarrhea and fatigue. In most cases, these AEs are of low grade, but as illustrated by the example, they can be significant enough to impact the patients' quality of life and lead to the withdrawal of the treatment¹⁵. There are certain recommendations for the use of anti-PD-1 monotherapy and they are contraindication to TKI or anti-VEGF agents, uncontrolled hypertension, recent cardiovascular diseases or Child-Pugh B status. However, a single agent of PD-1 or PD-L1 inhibitor has not gotten its approval as a first line systemic therapy. Liver cancer, or more specifically hepatocellular carcinoma (HCC) is the sixth most frequent cancer and the third cause of mortality by tumor. Most of the HCC are staged in Asia and HBV infection is the leading cause of HCC in the world

accounting for 50-70% of all cases¹⁶. Thus, even though the diagnosis is made in an earlier stage nowadays, the majority of patients with HCC come to medical care with the tumor at an advanced stage, and this substantially reduces radical surgical treatment options. In the worldwide setting, tyrosine kinase inhibitors (TKIs) using sorafenib and lenvatinib are suggested first-line therapy for uHCC¹⁷. There is still a large untapped potential for TKIs in terms of the size of the patient population that could be helped by a therapeutic. Lately, immune-oncology with immune-checkpoint inhibitors (ICIs) has entered the management of advanced HCC and changed the concept. Co-administration with an ICI is synergistic with a TKI since the latter may affect VEGFR and other kinases that may affect the mechanism of action of the ICI¹⁸. Globally, the phase 3 trial named LEAP-002 compared the effectiveness and safety of lenvatinib plus pembrolizumab as the initial treatment in uHCC patients. While dantleinb did not reach its bid primary endpoints of OS and pfs, as well as the key secondary endpoint of cRCC in the ITT population, subgroup analysis indicated median OS, and PFS trend favoured the combination over lenvatinib alone in Asian patients with high prevalence of HBV-related aetiology^{19,20}.

CONCLUSION

This review highlights the potential of tislelizumab plus lenvatinib as an effective first-line treatment option for patients with unresectable HCC. The combination of tislelizumab and lenvatinib offers a promising first-line treatment option for patients with unresectable HCC, demonstrating significant improvements in overall survival and progression-free survival with a manageable safety profile.

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