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EDITORIAL

EVOLUTION IN TEACHING METHODOLOGIES IN MEDICAL EDUCATION AND TRAINING

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With the introduction of the concepts of curriculum integration, contemporary educational methodologies, assessment tools, and the teaching methods in medical education, both undergraduate and postgraduate, have transformed significantly in the last 2 decades in Pakistan.[1] Traditional long lectures, blackboards/whiteboards, lecturing at the bedside, true false MCQs, long essay questions, and traditional viva were part of the assessments in those years. There was no concept of a structured teaching and assessment method.[2] Due to innovation in teaching methodologies and assessments, these methods are either vanished or towards that fate. The next sections will highlight the transition of these teaching tools, teaching methods, and assessment techniques from an archaic design to a contemporary one.

Teaching tools: Before the introduction of computers and the internet, in the late 20th century, an overhead projector, a manual slide changing machine, and a white screen hanging over the wall in front of the students were used to be the teaching tools in a classroom.[3] Even those gadgets are considered to be modern if one recalls the use of 'recitation' as a way of teaching and learning in front of the whole class. Students would sit in silence, while one student after another would take turns to recite the lesson until each one had been called upon. The teacher would listen to each student's recitation, and they were expected to study and memorize the assignments. At the end of the session/module, a written test or oral examination would be conducted; this process was called an Assignment Study Recitation Test.[4] It was followed or coincided with chalkboards which are still used in many classrooms especially by teachers with traditional mind-sets.

Then came the era of overhead projectors and slides. When PowerPoint was introduced in 1987, presentations changed forever.[5] It wasn't long before the presentation software took over and tools like overhead projectors and slide carousels became storage room trash. Before slides were designed on computers, they were made by hand. It used to take several days to design a slide deck and it was really expensive. Back in those days, presentations were visualized with tools like paper flip charts and slide projectors, and these were used in classrooms and meeting rooms all over the world. In the modern world, one cannot think of a presentation without a PowerPoint or other electronic medium.

Teaching methods: The modes of teaching included the model of apprenticeship, where a more learned teacher teaches less leaned students through hands-on training or indirect teaching and observations.[6] This mode is still prevalent in many disciplines in medicine, arts, industry, and others. The information thus gained is applied by the students in practice.

There came the era of lecture-based teaching which is considered to be one of the more cost-effective and convenient methods and is prevalent throughout the world in undergraduate medical education and other disciplines. However, some of the limitations of this form are; lesser interest of students, least retention of knowledge in the minds of students, and passive way of transferring knowledge.[7] The world in the late 20th century moved to small group teaching in the form of problem-based learning, team-based or task-based learning techniques. Although more effective in terms of knowledge retention and skills acquisition, these techniques require more expertise and resources.[8] The undergraduate medical education in Pakistan, going through curriculum reforms, is transforming its shape from archaic, traditional, and mostly lecture-based teaching methods to one of the small group teaching methodologies.

Workplace-based teaching and learning: In the past, bedside teaching in medical training at the undergraduate level and even postgraduate, used to be transferring a lot of information, and enforcing rote memorization by the teachers. The teacher used to stand at the bedside for hours and used to teach students the theoretical and practical aspects of a topic. However, with the inculcation of new bedside teaching techniques, the concept of one-minute preceptor and SNAPPS model of teaching was introduced, which has transformed the teaching methodologies from one with rote memorization to the contextual one, case-based and using the techniques of critical thing and clinical reasoning abilities of students.[9]

Online teaching and learning: Although, this form of teaching remained prevalent in the western medical institutions for the last 2 decades, but became more im-

portant recently in the era of Covid-19. The challenges of lockdowns, fear of waste of educational time of students and pressure of the society and government, the medical teaching institutions in the country started this form of teaching through web-based educational platforms like Zoom, Google Meet, MS Team and others.[10] It is expected that even without Covid-19 pandemic, this form of teaching will become universal even in third world countries in a decade or two, and will surpass the time taken for face to face teaching in the colleges and universities.

Assessment techniques: With the advances in assessment methodologies, drastic reforms have been introduced in the curriculum and assessment. Some of the examples are, conversion of long assay type questions into small short answer questions, true-false MCQs to one best answer MCQ, extending matching questions (EMQs), and Key feature format questions to enhance the clinical reasoning and clinical decision-making skills of students.[11] The students, instead of waiting for months for their results to be announced, get their results in a few hours, or maximally days. The traditional viva, where the unfortunate first comers in the viva used to be grilled a lot, has been converted into a more structured, task-oriented assessment of skills, traditionally called OSPEs and OSCEs.

In the era of curriculum reforms for undergraduate medical education and training, progressively, intentionally, or unintentionally, the methods of teaching and learning and assessments of medical students are undergoing a paradigm shift. These transformations are not without challenges. The most important stakeholder in these reforms is the teacher and student who are the end-users of these technologies. Another one is a challenge to the curriculum designers and policymakers, where the lack of expertise, facilities, and equipment as important frame factors, cannot cope with the demand. The mind-sets of teachers, students, and even society will need time to shift from the old teaching and learning and assessment techniques to contemporary ones.

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ORIGINAL ARTICLE

CORRELATION OF SEVERITY OF DISEASE AND CHANGES IN BASIC HEMATLOLOGICAL PARAMETERS IN PATIENTS OF COVID -19

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ABSTRACT

Objective: To determine the correlation between disease severity and changes in basic hematological parameters in cases of Covid-19 in a tertiary care center.

Materials and methods: This Cross Sectional analytical study was done in Khyber Teaching Hospital from March to June 2020. Covid-19 cases diagnosed by nasal swab PCR were included in the study. Clinical features were noted by doctor on duty and complete blood count was done. Data was analyzed by SPSS. Mean and standard deviation were used for quantitative data. Frequency and percentages were used for qualitative data. Shapiro Wilk's test was done to find normality of the data. Rank biserial correlation test was applied to determine association between ordinal (decreased, normal and increased cell counts) and dichotomous (severe and non-severe disease) variables. Levels of hemoglobin leukocyte count and platelet counts in severe cases were shown by box plots.

Results: Mean age of 101 cases of Covid-19 was 56±15.7 years. Male to female ratio was 1.5:1. Commonest clinical features were generalized body aches and fever, seen in 53(52.5%) and 48(47.5%) cases respectively. 36 (35.6%) cases were serious and needed ventilatory support. In serious cases, hemoglobin and platelet count was normal in most of the cases i.e. 16(44.4%) and 30(83.3%) respectively, while the leukocyte count was increased in 26 (72%) which was statistically significant (p=.017, OR=1.124).

Conclusion: Leukocyte count is high in cases of Covid-19. There is no significant correlation between severity level and hemoglobin and platelet count. The raised total leukocyte count is associated with severe disease in Covid19.

Key words: Covid-19, hemoglobin, platelet count, leukocyte count.

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INTRODUCTION

Covid-19 is a viral disease that appeared for the first time in China in December 2019 [1, 2]. It is caused by a bat virus called Corona virus [1]. The disease spread like fire to infect people all over the world in less than an year[3]. So far, no effective treatment could be discovered for this disease [3]. The World Health Organization (WHO) has suggested to call the virus as "2019 novel coronavirus" (2019–nCoV) [1]. So, the virus causing this pandemic is called "coronavirus disease 2019" (COVID–19) according to the guidelines of W.H.O [1, 2] In Pakistan, Covid-19 is spreading very fast [4]. This is because Pakistan has trade with China and Iran, and also because of travelling activities of the people [4]. It was February 26, 2020 when first case of Covid-19 was identified in our country [4]. Gradually, from there it spread from city to city and now it has reached every corner of the country [4]. Pakistan had confirm approximately 4600 cases of Covid-19 just within one month of the first case [4].The attack rate of Corona virus is 2.3 per 100 000 in Pakistan[4]. About half the cases of Covid are reported from Punjab [4].The second highest number of case are reported from Sindh , followed by Khyber Pakhtunkhwa [4]. The lowest number of cases of Covid-19 is reported from Azad Kashmir, followed by Islamabad [4]. The recovery rate of Covid -19 is highest in Gilgit Baltistan area [4]. In Pakistan, the distribution of Covid 19 is about 70% male and 30% females [4]. People of young age are effect-

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ed more commonly [4].Clinical features of Covid 19 have gradually been discovered as more and more patients were studied [3].Generally, it is reported that the disease may range in severity from asymptomatic state to severe disease requiring ventilator support[5]. In its asymptomatic form, the patient has no complaints and no findings are seen on chest X rays [6-8].Although they do not have any symptoms, yet they can spread the disease to others . In cases having severe disease, patients have high grade fever , cough, difficulty breathing, loss of sense of smell and body aches and pains[3].

The hematological parameters change in Covid 19 and thus help in early detection and monitoring of the disease [3].The most commonly effected parameters are white cell count and platelet count [9]. Covid 19 patients have decreased white cell count, and in that too lower lymphocyte count [3, 9]. Understanding the reason of these changes in hematological parameters can help us discover the pathophysiology of the disease[3].

Also, the hematological parameters need to be monitored in order to timely determine which patients need to be shifted to ICU as serious patients have more severe drop in cell counts [10]. Therefore, we planned to conduct this study in order to determine the correlation between severity of disease and changes in basic hematological parameters in cases of Covid 19 in Peshawar .

MATERIALS AND METHODS

This was a Cross sectional analytical study conducted in Khyber Teaching Hospital, Peshawar , from March 2020 to June 2020 . Ethical approval was obtained from institution's Ethical Board. Cases of Covid 19 as diagnosed through nasal swab PCR at Khyber Teaching Hospital were included in the study. Sampling was done by Non probability purposive sampling. The Clinical features were recorded by the Doctor on duty and the Complete blood count was done in Pathology department. The clinical features and hematological parameters were recorded in a proforma. Data was analyzed using SPSS. Mean and standard deviation were used for quantitative data while frequency and percentages were used for qualitative data. Shapiro Wilk test was used to determine normality of the data so as to determine whether parametric or non- parametric test should be applied on variables. The correlation between binary (severe versus non severe disease) and ordinal (decreased, normal and increased counts) variables was determined by applying rank biserial correlation test. Changes in hematological parameters were shown by bar graphs and tables and box plots. Logistic regression model was used to predict the severity level from levels of hemoglobin, leukocyte count and platelet counts taking into account odds ratio and confidence level of 95%. *P*-value of less than 0.05 was taken as statistically significant.

RESULTS

A total of 101 cases of Covid 19 were included in the study. Age range of the study population was 16-95 years, with mean of 56 ±15.7 years. Gender distribution is shown in figure 1. Clinical features of study sample are shown in figure 2. Changes in hematological parameter are shown in table 1. Changes in hematological parameter in severe cases of Covid 19 are shown in table 2 and figure 3. The strength of association between basic hematological parameters and severity of the Covid 19 is shown in table 3 .Table 4 shows results of logistic regression.

Table 1: Changes in hematological parameters in study sample (n=101)

Basic Hematological parameters	Mean ± SD	Range	Decrease n(%)	Normal n(%)	Increased n(%)
Hemoglobin (gm/dl)	1.86±12.3	7-15	47(42.6%)	43(42.6%)	11(10.9%)
Total leukocyte count (x103/L)	4.8±12.4	3.4-31.9	3(3%)	44(43.6%)	54(53.5%)
Platelet count (x103/L)	240.3±103.4	84-790	11(10.9%)	86(85.1%)	4(4%)

Table 2: Changes in hematological parameters in severe cases of Covid 19 (n=36)

Basic Hematological parameters	Mean ± SD	Range	Decreased n(%)	Normal n(%)	Increased n(%)
Hemoglobin (gm/dl)	12±1.8	8-15	19(52%)	16(44.4%)	1(2.8%)
Total leukocyte count (x103/L)	13±4.7	3.9-28	1(2.8%)	9(25%)	26(72%)
Platelet count (x103/L)	236±89.5	84-460	5(13.9%)	30(83.3%)	1(2.8%)

Table 3: Severity of ED in Diabetic Patients

Association	Rank biserial correlation value	p-value*
Between severity level and hemoglobin level	-.160	.111
Between severity level and leukocyte count	.254	.011
Between severity level and platelet count	-.082	.415

Table 4: Logistic regression analysis for predicting severity of Covid 19 from hematological parameters

Variables	Beta coefficient	Standard error	Walds test statistic	p-value	Odds ratio	95% confidence interval	
						Upper limit	Lower limit
Hemoglobin	-.202	.118	2.910	.088	.817	.648	1.030
Total leukocyte count	.117	.049	5.698	.017	1.124	1.021	1.238
Platelet count	-.002	.003	.862	.353	.998	.993	1.803

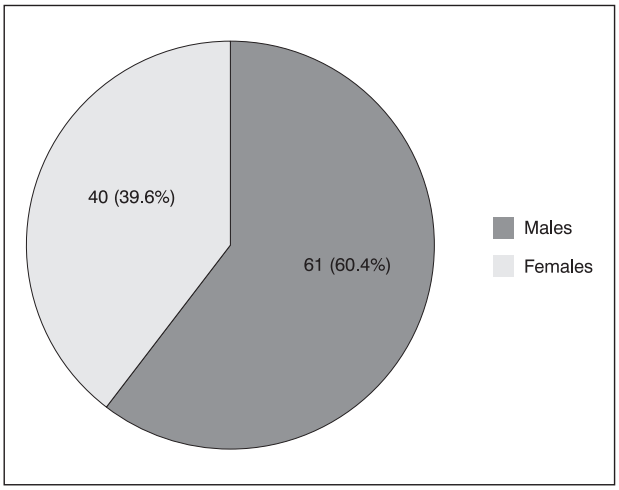


Fig 1: Gender distribution in study sample (n=101)

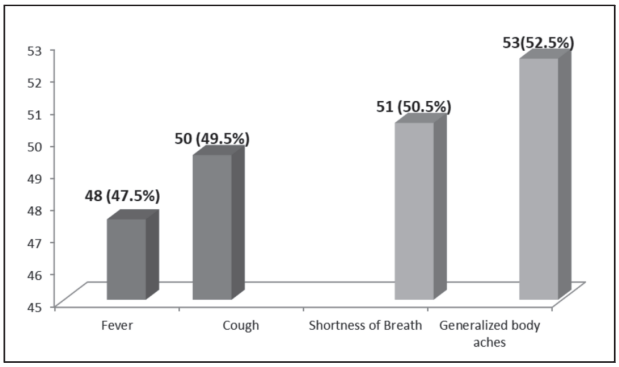
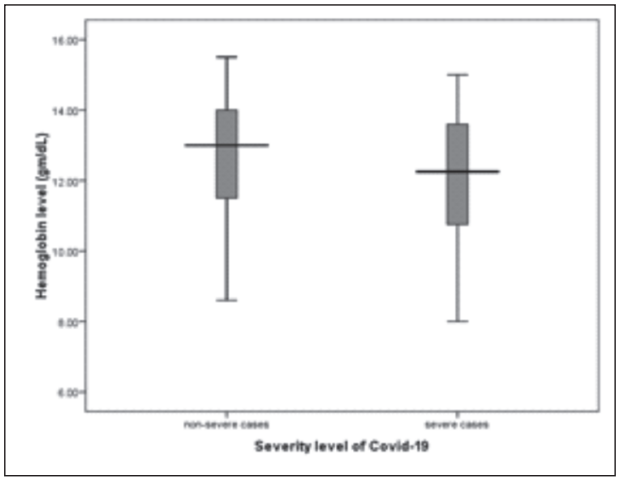


Fig 2: Clinical features in patients of Covid 19 (n=101)



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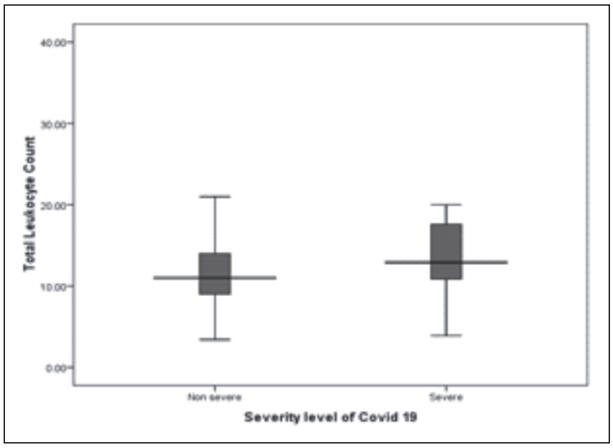

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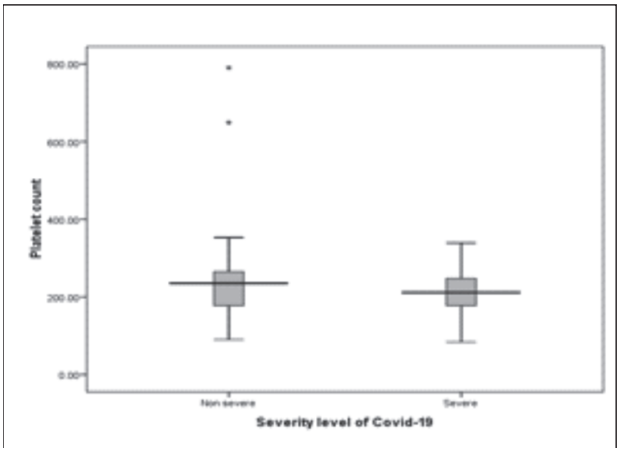

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Figure 3: Box plot showing level of hemoglobin (a), leukocyte count (b) and platelet count (c) in severe versus non severe cases of Covid-19

DISCUSSION

The present study showed that Covid-19 was common in old age and more common in male population. Guan presented the median age of the patients with Covid-19 as 47 years; and reported that it was common in males [11]. Similarly , a meta-analysis done recently reported that the Covid-19 infection is common in males as compared to females [12].

In the present study, it was seen that the commonest clinical feature in patients of Covid-19 was generalized body aches, cough and fever. Similar findings are report-

ed in a meta-analysis , reporting that the commonest clinical features of Covid-19 are fever and cough [12].

In the present study, hemoglobin level and platelet count were normal in majority of the patients of Covid 19, and there was no association between severity level and hemoglobin level (p=.088, OR=.817, CI= .648-1.030) and platelet count (p=.353, OR=.998, CI=.993-1.803). Leukocyte count was raised in majority of the cases in the present study and raised leucocyte count contributed significantly to severity level in logistic regression model in our study (OR=1.124, p=.017, CI=1.024-1.238). This finding is same as that reported in literature. Huang C from China reported that the patients having severe disease is associated with rise in leukocyte count [9]. Similar data is presented by Wang in his study[13]. However , Chang in his study showed that there was no significant change in leukocyte count in patients of covid-19 [14] . In a meta-analysis done recently , it was reported that majority of Covid 19 patients (about 64%) had normal leucocyte counts [12]. When lymphocyte count is considered , it is reported that Covid-19 is associated with low lymphocyte count [15, 16].It is also reported that low lymphocyte count is associated with increased risk of death [13] .However we could not include data on lymphocyte count in our study. It is also reported that a raised ratio of neutrophil to lymphocyte count is associated with severe disease [17]. However, we could not work on neutrophil to lymphocyte ratio in our study.

Most of the studies done so far has shown that the red cell lines are not effected in Covid 19 [9, 11, 15, 17-21]. In all these studies, no change was found in red cell parameters, neither in severe cases, nor in mild or moderate cases .These are findings same as that reported in the present study where there was no association between hemoglobin level and disease severity. However , in a meta-analysis done by Mattiuzzi, it was shown that a low hemoglobin level is associated with severe Covid 19 [22].

When platelet count is considered, most of the studies done so far have shown that there is no significant change in platelet counts in Covid 19 patients , neither there is a difference in platelet count between severe and mild cases [9, 13, 17, 19-21] .This is same as that in the present study where there was no association between change in platelet count and disease severity. However, in one study involving a very large number of patients i.e. 1099 covid-19 cases , it was shown that the platelet count was reduced in 57% of the patients in severe cases [11].Lippi et al have reported that a decreased platelet count hints at serious condition [23]. The exact reason for this low platelet count in Covid 19 serious cases is not known so far[3].

The study was conducted only at one center . So, the result may not be generalized .Also , we could not determine the association of severity level of Covid-19 with lymphocyte count , and neutrophil to lymphocyte ratio.

CONCLUSION

Hemoglobin levels and platelet count are normal in most of cases of Covid-19, while leukocyte count is raised .There is no association between severity of the disease and hemoglobin level, and platelet count. However, a weak association exists between raised leukocyte count and severity level in Covid-19.

We recommend that further work should be done to determine the relationship between leukocyte count and severity level of Covid-19. Also, the hemoglobin level and platelet count should not be used to assess severity level in Covid-19.

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AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under

Khan MI: Conceived the idea, data collection, write up

Mehmood M: Statistical analysis, results.

Husain SO: Literature search.

Waqar S: Bibliography.

Asim M: Data collection.

Rehman N: Writing discussion.

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

ORIGINAL ARTICLE

PERCEPTION OF POSTGRADUATE FAMILY MEDICINE TRAINEES ABOUT THE OBJECTIVE STRUCTURED CLINICAL EXAMINATION (OSCE) ASSESSMENT METHOD

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ABSTRACT

Objectives: Assessment drives learning and improving the quality of assessment has a remarkable impact on the quality of learning. Objective Structured Clinical Examination is termed more reliable and valid as compared to conventional practical examination.

Objective: The objective of this study was to find the perception of postgraduate family medicine trainees about the OSCE assessment method and compare those having previous experience with those having no previous experience.

Material & Mothods: This was a cross-section study conducted at the end of exit examination of diploma in family medicine at the Family Medicine Department, Khyber Medical University Peshawar. Data were collected on an eleven items questionnaire on a five-point Likert Scale. Study participants were categorized based on their previous experience of the OSCE, and were grouped into two categories. Data were analyzed by using Fisher's Exact test and a p-value of ≤ 0.05 was considered statistically significant.

Results: Out of 60, 56 candidates returned completed questionnaires. The response rate was 93.33% where the majority were males 52(92.9%). Participants with experience of the OSCE were 22 (39.3%) while 34 (60.7%) were having no experience of the assessment method. There was a significant difference ($p= 0.001$) in the perception about the OSCE with the simulated patient than real patient, fairness and reliability of the OSCE, stress and length of the OSCE and reduction of bias in the OSCE. The perception about weightage to be given to the OSCE in any examination was significantly different ($p=0.004$) between the two groups.

Conclusion: Participants of both groups (experienced vs non-experienced) agreed on some aspects of the OSCE. Their opinion differed about the fairness, validity and stress related to the OSCE assessment method. This difference is probably explained by the inadequacy of an experience to form an opinion.

Keywords: Conventional practical examination, Family medicine, OSCE.

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INTRODUCTION

Assessments have a steering effect on learning in medicine and current notion is "assessment for learning" rather than "assessment of learning" [1, 2]. Students usually study that part of the course that is going to be assessed. Their learning usually depends on their thinking of the assessment method[3]. Assessment must have both educational and formative role to help the students learn and develop practical skills. However, to keep specific standards and assurance of public, it is also necessary to have summative test of the doctors performance [4]. Inaccuracies in the knowledge judgement, practical skills and doctors attitude may pose some risk to the patient [5]. The effective and efficient healthcare delivery requires sound knowledge of the subject, practical skills, analytical skills, communication skills, counseling and evidence- and system-based care. All these skills require an assessment method that is comprehensive, robust and reliable to assess these required attributes [6].

For a credible and reliable assessment in medi-

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cine, it is essential not only to assess clinical knowledge and skills but professionalism and empathy also. Improving assessment has a remarkable impact on the quality of learning. Over the last two decades the evaluation of clinical performance has evolved and structured methods of assessment like Objective Structured Clinical Examination (OSCE) were introduced. OSCE was introduced by Harden in 1979 and now is used as a most valid method of clinical competence assessment in most medical examinations [8, 9]. OSCE can test a wide range of skills which reduces sampling errors and improves the reliability of examination [9].

In the course of Diploma in Family Medicine, OSCE was introduced as form of summative assessment. In Pakistan students and trainees are more familiar with the traditional forms of clinical assessment like long case and short cases during their course of study and training. OSCE was introduced to overcome the unreliability and lack of standardization in long case [5, 9].

The problems with traditional short cases and long cases are that performance depends on candidate's presentation. It makes it an assessment at "knows how" rather than "shows how" so not as reliable and authentic for clinical competence assessment. Only one long case and three or four short cases are used so only limited clinical skills can be assessed [10].

In the diploma course, the expected level of skills was decided to at least at "shows how" level of the Millar's pyramid. According to Miller the traditional assessment of medical students was much focused on testing their knowledge and assessment did not reflect on how they would behave in a real-life workplace [11, 12].

Despite the facts about the unreliability of their traditional format of assessment, there may still be some anxiety to try a different mode of assessment they have never used before. Students who have been previously exposed to OSCE, preferred OSCE as method of assessment for clinical competence as compared to traditional clinical examination [13]. The objective of this study was to compare if comprehensive OSCE assessment, is as useful and reliable for assessment of Diploma Family Medicine students who are not exposed vs those exposed to this format of examination during their undergraduate and postgraduate training. The intention of using OSCE is to test their knowledge, attitudes, and skills to reach a summative decision to allow them to be fit to practice as independent family physicians.

MATERIAL AND METHODS

This was a cross-section analytical study conducted at Institute of Public Health and Social Sciences, Department of Family Medicine, Khyber Medical University Peshawar. Ethical approval was sought from the institute ethical review board. The study was conducted in 2019 and 2020 at the end of exit examination of Diploma in Family Medicine.

The diploma in Family Medicine is one year program with six modules and five mandatory clinical rotations. There is an OSCE examination at the of each module. There is an exit examination at the end of all modules. There are 12 stations, covering wide range of psychomotor and affective skills from the curriculum. Time allotted to each OSCE station was 15 minutes with 1 minute transition time between stations. Performance at each OSCE station was scored according to the checklist for that OSCE with items covering key skills for that station. Range of items on check list was between 10 and 20.

A questionnaire comprising of 11 questions was developed based on constructs identified from the literature and was expert validated to eliminate or rephrase ambiguous questions. The questionnaire evaluated perception of the recently completed OSCE using a 5-point Likert scale with strongly agree (score of 1) at one end and strongly disagree (score of 5) at the other end.

The total population census was carried out to avoid loss of information because of small sample size. The participants were asked to complete a self-administered questionnaire after seeking informed written consent. The 56 out of 60 participants completed the questionnaire. Response rate was 93.33%.

Data was analysed in Stastical Package for Social Sciences (SPSS) version 24. Age was calculated as mean and categorical variables; gender, years of education, duration in clinical practice, qualification, previous exposure to OSCE and formal training in the past were calculated as frequency and percentages. Five-point Likert scale was collapsed into 3 points scale (agree/strongly agree, neutral and disagree/strongly disagree) for the purpose of analysis. The response to 11 items on Likert scale was calculated as frequencies on each point for an item. Each item was compared by Fisher's Exact Test according to whether candidates had experience of being evaluated by OSCEs in the past or not. The Fisher Exact test was used for 2 x 3 contingency tables. This method was preferred to calculate p value for a small sample size and some cells having frequency less than five[14]. Results were displayed in tables. P-value of ≤ 0.05 was considered significant.

RESULTS

The total 56 participants were dominated by males 52(92.9%). Mean age of study participants was 35.07 years. The participants with basic medical qualification like MBBS/MD were in majority 42(75%). The participants with postgraduate qualification were 16 (28.6%). Half of the participants were currently involved in clinical practice and out of this28 (50%), 16(28.24%) in clinical practice for seven or more years. The participant who had received formal training in clinical medicine constituted 8(14.3%),

Table 1: Descriptive statistics of the study participants

Gender	Male	Female		
	52 (92.9%)	4 (7.1%)		
Age (years)	Min	Max	Mean	SD
	28	43	35.07	4.29
Years of education	16years	18years		
	42 (75%)	14 (25%)		
Qualification of Participants	MBBS/MD	MCPS	MPH	MPhil
	40 (71.4%)	2 (3.6%)	12(21.14%)	2 (3.6%)
Currently in clinical practice	Yes	No		
	28 (50%)	28 (50%)		
Duration of clinical practice of 28 participants	< 7 years	≥ 7 years		
	12 (20.7%)	16 (28.24%)		
Exposed to OSCE previously over course of education	Yes	No		
	22 (39.3%)	34 (60.7%)		
Formal training received before	Yes	No		
	8 (14.3%)	48 (85.7%)		

Table 2: Likert scale questionnaire and data analysis by Fisher Exact Test

	Question	Exposure to OSCE	SA/A	N	DA/SDA	EET p-value	Test statistics
1	OCSE with SP better than RP in ward	Yes	20 (90.90%)	0 (0%)	**2 (9.10%)**	**0.001**	**16.92**
		No	14 (41.17%)	10 (29.41%)	10 (29.41%)		
2	OSCE is fair and reliable as compared to CPE (viva, long case, short case)	Yes	20 (90.90%)	0 (0%)	2 (9.10%)	0.001	17.39
		No	20 (58.82%)	14 (41.17%)	0 (0%)		
3	OSCE covers a wide range of knowledge and skills	Yes	20 (90.90%)	2 (9.10%)	0 (0%)	0.455	1.44
		No	28 (82.35%)	6 (17.64%)	0 (0%)		
4	OSCE is fair to mark performance scores for examiner	Yes	12 (54.54%)	10 (29.41%)	0 (0%)	0.782	6.12
		No	20 (58.82%)	14 (41.17%)	0 (0%)		
5	Time allocated to each OSCE station is adequate	Yes	18 (81.81%)	2 (9.09%)	2 (9.09%)	0.151	20.13
		No	20 (58.82%)	4 (11.76%)	10 (29.41%)		
6	OSCE is more stressful as compared to CPE	Yes	16 (72.72%)	0 (0%)	6 (27.27%)	0.001	22.46
		No	10 (29.41%)	16 (47.05%)	8 (23.52%)		
7	OSCE is lengthy as compared to CPE	Yes	10 (45.45%)	0 (0%)	12 (54.54%)	0.001	23.98
		No	4 (11.7%)	18 (52.94%)	12 (35.29%)		
8	OSCE is useful to assess psychomotor domain	Yes	18 (81.81%)	4 (18.18%)	0 (0%)	0.845	0.62
		No	28 (82.35%)	6 (17.64%)	0 (0%)		
9	OSCE reduces bias by examiner as compared to CPE	Yes	16 (72.72%)	6 (27.27%)	0 (0%)	1.00	14.44
		No	12 (35.29%)	16 (47.05%)	6 (17.64%)		
10	Adequate weightage should be given to OSCE in any examination	Yes	22 (100%)	0 (0%)	0 (0%)	0.004	13.90
		No	24 (70.58%)	10 (29.41%)	0		
11	OSCE should be continued as evaluation tool for any clinical programme	Yes	20 (90.90%)	2 (9.10%)	0 (0%)	0.285	2.12
		No	26 (76.47%)	8 (23.52%)	0 (0%)		

Note: SA (Strongly agree), A(Agree), N (Neutral), DA (Disagree), SDA (Strongly disagree), SP (simulated patient), RP (Real patient), CPE (Conventional practical examination) FET (Fisher's Exact Test),

MEC (Minimum expected count in cell)

irrespective of whether the training resulted in successful completion of postgraduate degree or not. The participants who had experience of being evaluated by OSCE, whether in graduate school or post-graduation constituted 22 (39.3%) as opposed to 34 (60.7%) who only had experience of conventional clinical examination in the form of short and long cases (Table-1).

The response to question whether OSCE with simulated patient (SP) is better than real patient (RP), demonstrated significant difference with a p-value of 0.001. The participants with experience of OSCE in the past were more in agreement with statement than those with no exposure to OSCE previously. Similar differences ($p = 0.001$) were seen in comparing fairness and reliability of OSCE, stress of OSCE, reduction of bias in OSCE vs Conventional Practical Examination (CPE). Opinion regarding weightage to be given to OSCE in any examination was significantly different ($p = 0.004$) between two groups (Table-2).

DISCUSSION

The OSCE method of assessment is a recognized and commonly used tool in postgraduate medical education [15]. The aim of the study was to know the opinion of those who have not experienced OSCE in their undergraduate education and compare it with those who have had such experience. This feedback will help guide in successful implementation of OSCE in Diploma course of Family Medicine[16, 17]. Keeping in view the 93.33% response rate, bias is unlikely thus giving strength to this study.

The both groups participants agreed on that OSCE is suitable for assessing wide range of knowledge and skills, specially psychomotor skills as supported by literature[17, 18]. Both the groups also agreed that OSCE is easy to score for examiner, reduces bias by examiner and each OSCE station gets sufficient time for the task assigned[18]. They agreed on OSCE being part of any evaluation programme in clinical medicine. Similar opinions were expressed by Pharmacy students and undergraduate students [18,19-21]

As compared to undergraduate students who took OSCE in Family Medicine and had no experience of OSCE before, gave positive response to majority of the aspects of OSCE[17]. In contrast to undergraduate students in Family Medicine, participants differed on the opinion that OSCE is better with simulated patient, fair and reliable. Majority of literature has reported otherwise in regard to fairness and reliability of OSCE[17, 18, 22-24]. These differing opinions might be explained by the fact that one experience of OSCE might be inadequate to form an opinion about these aspects of OSCE [17].

The group with no prior experience of OSCE had significantly different opinion regarding weightage to be given to OSCE in any examination, in alignment with their doubts about its fairness and reliability. The group with prior OSCE exposure stated that OSCE examination takes more time as compared to CPE.

The difference in opinion was also observed regarding stress caused by OSCE. Surprisingly the group with no prior experience of OSCE termed it less stressful as compared to CPE. This might be explained partly by the fact that it was their first experience and they were briefed about the process of OSCE before examination, that might not be there in CPE [17]. The more stress expressed by participants with past exposure to OSCE may be attributed to their knowledge of objective and standardized nature of OSCE and the ability of OSCE to assess competencies other than as assessed by CPE. This aspect of OSCE needs good practice and may be the reason of stress among participants[18]. The test anxiety and stress is higher with OSCE as compared to other forms of assessment but has no or minimal influence of performance [25]. Providing training to all those involved and make them aware of any potential problems will make the OSCE run smoother, and students will adopt it quickly easier.

CONCLUSION

Participants of both groups reported OSCE as a positive experience that provide an opportunity to practice real life scenarios[21]. The differences in opinion between two groups regarding fairness, validity and stress related to OSCE, is probably explained by inadequacy of one experience to form opinion.

LIMITATIONS

Small number of female candidates in the study and study could not explore the effect of gender and personality on scoring OSCE assessment. This was a single centre study and involved participants of one speciality thus limiting generalization.

RECOMMENDATIONS

The In-depth qualitative exploration of doubts regarding fairness, reliability of OSCE and less stress as compared to CPE, by participants with no prior experience of OSCE need further exploration.

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AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under

Khan AJ:	Main idea, data collection and manuscript writing
Adeeb H:	Data collection, statistical analysis and manuscript writing
Ullah I:	Literature review, Methodology, Manu script writing and critical review
Jamil B:	Manuscript writing, Critical expert review and corrections
Samin KA:	Manuscript writing, discussion and Critical review
Jawad M:	Data collection, Manuscript writing, intro duction and references

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

ORIGINAL ARTICLE

EXPLORATION OF BARRIERS PERCEIVED BY ONCOLOGY NURSES RELATED TO CANCER PAIN MANAGEMENT

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ABSTRACT

Objectives: To explore barriers perceived by oncology nurses in cancer pain management.

Methods: A descriptive Cross sectional study was conducted in oncology department of four tertiary care hospitals of Punjab which include Mayo hospital Lahore, Jinnah hospital Lahore, Allied hospital Faisalabad and Nishtar hospital Multan. Sample size was calculated as 72 nurses by using WHO formula. Subjects were selected by purposive sampling technique from nurses working in oncology departments of four tertiary care hospitals. Research tool was adopted from previously published study with ethical permission. The data analysis was performed using SPSS version 20 and Microsoft excel. Descriptive statistics were used to analyze data.

Results: Four domains were covered in the results for exploration of barriers perceived by oncology nurses. Results showed that 97.3% nurses considered the lack of pain management training as barrier in pain management. From patient perspective, mood alteration of patient was responded by 87.7% nurses as barrier. 84.8% nurse perceived unavailability of physician at the time of pain as barrier and 95.9% perceived inappropriate nurse-patient ratio as barrier.

Conclusion: System related barriers were found more prevalent in cancer pain management from which inappropriate nurse –patient ratio was concluded most agreed barrier.

Key words: Pain, cancer pain, pain assessment, pain management, barriers

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INTRODUCTION

Cancer is a global health problem and second leading cause of death [1]. All over the world in 2020, there were an estimated 19.3 million new cases of cancer were reported, out of which roughly 10.0 million were pronounced dead [2]. In Pakistan, the incidence of cancer is estimated at 148,041 per year. During the period of last five years over 100,000 deaths due to cancer was reported and prevalence of diagnosed patients were 350,000 [3]. Although patient with cancer presents with multiple symptoms but pain is most predominant and distressing symptom of cancer that affects the quality of life of patient as well as family in all aspects. Not only the disease of cancer is painful but the treatment like chemotherapy is also pain full that creates hindrance in the prognosis of disease.

This lead to many complications such as anxiety and sleep disturbance and increase patient stay in hospital [4]. Despite of persistent work done on pain management and introduction of advance therapies only slight improvements have been achieved and still 45.6 % of the patients reported pain in early stage of cancer while 73.9 % of the patients reported severe pain in advanced stage of cancer in many settings [5].

Oncology nurses are considered to have an obvious role in managing the pain of patients suffering from cancer. However, It is observed that nurses face multiple factors as barriers that cause them to inefficiently participate in assessment and management of pain [5-7]. These barriers are lack of pain management specialists in the health care team, improper nurse to patient ratio, religious and cultural misconception about the cancer pain [8]. Al-

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though many studies were conducted on pain management still there is limited data on the nurses' perceived barriers to optimal pain management in cancer patients in Pakistan. Hence this study is conducted to explore the barriers perceived by oncology nurses for the management of cancer pain.

MATERIAL AND METHODS

A descriptive Crossectional study was conducted in oncology department of four tertiary care hospitals including Mayo hospital Lahore, Jinnah hospital Lahore, Nishtar hospital Multan and Allied hospital Faisalabad from August 2019-December 2019. The sample size was calculated by WHO formula.

Equal numbers of subjects were selected from each hospital according to inclusion criteria. Female Nurses working in oncology department who had more than one-year general nursing experience and more than six-month experience in oncology department were include in this study.

Male nurses and LPN were excluded [18]. Permission was taken from ethical review committee and administration of hospital to conduct study. After taking permission data were collected from participants by questionnaire. The questionnaire was adopted from previously published study with ethical permission [9].

The reliability and validity of questionnaire was checked by one previous study and reliability value was found 0.8[10]. Four themes as nurses related, patient related, physician related and system related barriers were developed to explore the barriers in pain management. Likert scale was used to measure responses.

After the response of participants different numbers were assigned to the responses as 1 for agree, 2 for Neutral, 3 for Disagree in the questionnaire. After collection data was analyzed by SPSS version 20. Descriptive statistics test as-percentages and frequencies were used to analyse the data.

RESULTS

In this study Likert scale was used to assess the responses of respondents. Three degrees were used as agree, neutral and disagree. The responses more than 50% were considered as barriers. Table No 1 shows the analysis of the participants' responses on nurses'- related barriers. Table No 2 reveals the distribution of subjects according to patient related barriers. Table No 3 identifies the nurses' perception about physician related barriers. Table No 4 reveals the analysis of nurses' responses for institution related barriers.

Table 1: Nurse's related barriers

Age Group	Agree n%	Neutral n%	Disagree n%
Inadequate training to pain management	70(97.3)	2 (2.8)	0 (0)
Inadequate knowledge to pain assessment	51(70.8)	8(11.1)	13(18.1)
Inadequate knowledge to deliver nonpharmacological Intervention	51(70.8)	14(19.4)	7(9.7)
Reluctant to administer opiates due to strict narcotic policy	49(68)	5(6.9)	17(26)
Lack of time for health teaching to patients and their families	51(70.8)	10(13.9)	11(15.3)
Lack of proper pain assessment tools application	45(62.5)	6(8.3)	21(29.2)
Nurses indifference to patient's pain complains	38(52.8)	9(12.5)	25(34.7)

Table 2: Distribution of subject according to patient related barriers

Age Group	Agree n%	Neutral n%	Disagree n%
Patients have difficulty to rate their pain on pain scale	59(81.9)	12(16.7)	1(1.4)
Patients are reluctant to take medication due to fear of addiction	37(51.4)	5(6.9)	30(41.6)
Mood alterations produce difficulty for nurses to manage pain	63(87.5)	6(8.3)	3(4.2)
Patients prefer to report pain to doctor, but not to nurses	23(33)	8(11.1)	41(57)
Misconception that pain medication cannot control cancer pain	25(34.8)	9(12.5)	38(52.8)
Patients are afraid of being labeled as complainer	30(41.7)	6(8.3)	36(50)
Communication barriers	49(68)	11(15.3)	12(16.7)

Table 3: Distribution of subjects according to physician related barriers

Age Group	Agree n%	Neutral n%	Disagree n%
Shortage of time for proper pain assessment	44(61.1)	11(15.3)	17(23.6)
Reluctant to prescribe opiates because of the side effects	37(51.4)	9(12.5)	26(36.1)
Inadequate knowledge to assess pain	32(44.5)	17(23.6)	23(32.6)
Fear of legal and administrative constraint for opiate prescription	47(65.2)	8(11.1)	17(23.7)
Lack of pain management training to the physicians	12(16.7)	9(12.5)	51(70.8)
Unavailability of physician at the time of pain	61(84.8)	6(8.3)	5(6.9)
Physician's indifference	46(63.9)	16(22.2)	10(13.9)

Table 4: Distribution of subjects according to institution related barriers

Age Group	Agree n%	Neutral n%	Disagree n%
Lack of institutional policy and guide line for pain management	55(76.4)	6 (8.3)	11 (15.3)
Ratio of nurses are not according to patients	69(95.9)	3(4.2)	00(0)
Lack of non-pharmacologic therapy of pain Management (cold, hot, acupuncture etc.)	62(82.1)	09(12.5)	01 (1.4)
Strict Narcotic prescription regulation	47(65.2)	9(12.5)	16(22.3)
Lack of specialized pain management team	47(65.2)	3(4.2)	22(30.6)
Lack of psychosocial l support system to patient and family	64(88.9)	8(11.1)	00(0)
Lack of coordination across health care providers	46(63.9)	11(15.3)	15(20.8)

DISCUSSION

The current study was carried out to explore the barriers that nurses perceived in the management of cancer pain and have agreement with previous studies that nurse's related barriers exist and produce difficulty in pain management. Among nurse's related barriers, inadequate training to nurses for pain management, inadequate time for pain assessment, inadequate time for health teaching and non-pharmacological interventions were found most agreed barrier that put stress on the call for training of nurses on pain management [11-15].

With respect to patient related barriers, current study showed same results as previous studies reported that pain is often minimally or under report by patients for reasons based on their own understanding about pain scale. The results of this study contradict with the results of previous studies that pain management was a key responsibility of doctors and patients report pain to the doctors but not the nurses, also conceal their pain and refuse to take pain medication due to fear of addiction because in this study it was found that nurses were not considered these barrier [16-18].

The findings of this study also match with some previous studies that physicians have lack of time and knowledge to assess pain and also are reluctant to prescribe pain medication due to fear of addiction and strict institutional policies. Moreover it was found a great barrier that physician are not present at the time of pain [5,21,19].

Majority of studies concluded that Institution related barriers were most rated barrier in pain management. The results of this study match with previous studies, that lack of institutional policies, inappropriate nurse-patient ratio, unavailability of nonpharmacological measures produced hurdle in pain management and made nurses unable to control pain[13,20].

This study is restricted to cancer pain management. Further studies can be conducted on other perspectives of pain. A large sample size will be needed to validate the study. This study was confined to four tertiary care hospitals. It can be replicate with increased sample size and in other hospitals of Pakistan.

CONCLUSION

This study explored the barriers perceived by oncology nurses related to cancer pain management. The results of this study explored that from four groups of barriers institutional and nurses related barriers were found more prevalent. Among all these barriers inappropriate nurse-patient ratio was found most agreed barrier.

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AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under

Bibi T: Data collection writing

Begum R: Data collection and Review

Kausar S: Statistical analysis and Review

Farooqi S: Discussion writing and Review

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

ORIGINAL ARTICLE

COVID-19 PANDEMIC: HOW STRESSED THE STUDENTS AND FACULTY ARE?

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ABSTRACT

Objective: To assess the perceived stress levels amongst faculty and students of medicine, dentistry and allied health sciences during COVID-19 pandemic.

Material and Method: This multi-institutional descriptive study was conducted from April to June 2020. All the students and faculty from three institutes namely University College of Medicine, University College of Dentistry and the Institute of Allied Health Sciences were invited to participate. Data was collected using a pre-validated Perceived Stress Scale (PSS -10). descriptive and inferential statistics were calculated using SPSS v.21.

Results: 1199 responses were obtained. Students from the University College of Medicine reported higher scores on the Perceived Stress Scale (23.02+11.85) than those from the University College of Dentistry (21.87+10.86) and the Institute of Allied Health Sciences (21.95+11.32). The students and the faculty experienced stress 'sometimes to fairly often' during this pandemic. Females experienced more stress than males and there was no significant difference among students and faculty of various age groups.

Conclusion: During the COVID-19 pandemic, the students and the faculty from medicine, dentistry and allied health sciences institutes were moderately stressed. The medical students were more affected than the allied health and dental students. A higher stress level was reported among dental faculty as compared to the other two institutes. Institutions should hence promote resilience and mental well-being and provide for more flexible work schedules.

Keywords: Allied Health Sciences, COVID–19, Dentistry, Medicine, Mental Health, Pandemic, Stress

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INTRODUCTION

Coronavirus disease (COVID–19), an infectious disease caused by SARS-CoV-2 was first detected in Wuhan, China in late 2019. Within thirty days, the disease that presented as pneumonia of unknown cause was declared to be a public health emergency of international concern [1]. Within two months, over thirty thousand people had lost their lives to the pandemic. By August 4, 2020, over 18 million confirmed cases of COVID-19 had been reported, resulting in more than 691,013 deaths in 216 countries [1].

To slow down the progression of the disease and flatten the curve, many aggressive measures were taken which included travel restrictions, avoidance of social interactions, closure of academic institutions and other non-essential services such as private clinics, hospital OPDs and elective procedures. By April 2020, 192 countries had announced the closure of educational institutions, impacting 91.4% of the total enrolled learners [2]. This had a significant impact on the mental, physical and social well-being of learners [3].

To minimise the academic loss, Higher Education Commission (HEC), Pakistan issued guidelines on delivery of online courses [4]. As a result, most of the universities made a rapid transition from face to face, towards online teaching. Academicians reported this transition to be stressful as 'work from home' affected their work-life balance and teaching students remotely meant they had to find new ways to engage students academically [3]. Most of them were not familiar with online teaching tools required to ensure a meaningful learning experience for their students [5]. Likewise, this transition in the learning environment was difficult for students, who reported a limited attention span while taking online lectures. They also reported that while online learning offers some flexibility in terms of accessing learning material, it also limits the development of proficiency in certain domains of learning such as psychomotor skills [6]. While the younger generation maybe more comfortable with using technology as

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compared to the older generation, online teaching and learning poses its own challenges, especially in countries such as Pakistan where resources are constrained.

The potential ramifications of all the emergency measures taken during the COVID-19 pandemic cannot be ignored. These may have resulted in increased anxiety and stress among students and the faculty. To develop timely interventions for improving the mental, physical and social wellbeing, we need to establish this impact on the students and the faculty objectively. Hence, this study explores the perceived stress levels amongst faculty and students of medicine, dentistry and allied health sciences during the COVID-19 pandemic.

MATERIALS AND METHODS

This multi-institutional descriptive study was conducted from April to June 2020. Ethical approval was obtained from the Ethical Review Board, The University of Lahore (Ref# ERC/08/20/14 Dated 17th March 2020). Using convenience sampling, all the students (n=2850) and faculty (n=305) from three institutes namely University College of Medicine, University College of Dentistry and Institute of Allied Health Sciences were invited to participate using their Learning Management System (Moodle).

Data were collected using a pre-validated Perceived Stress Scale (PSS -10). The PSS-10 assesses the perceptions, feelings and thoughts of stress on 10 items using a five-point Likert scale (0=never, 1=almost never, 2=sometimes, 3=fairly often, 4=very often). It measures the degree to which life in the past month has been experienced as unpredictable, uncontrollable and overwhelming [7]. It has high reliability with Cronbach's alpha=0.79-0.82. Standard demographic questions were added, and the questionnaire was piloted with 10 students to ensure online accessibility and comprehensiveness.

Descriptive and inferential statistics were calculated using SPSS v.21. The total score was obtained by summing up the individual scores for all ten items. Four items (4, 5, 7, & 8) were positively worded hence their scores were reversed. A mean score of 2-4 for an item indicates sometimes to very often having such feelings/ thoughts during the last month. Frequencies and percentage were calculated for the demographic data. As the data was not normally distributed, therefore, Kruskal Wallis and Mann-Whitney U tests were applied to investigate the mean differences between institutions, students and faculty, gender and age groups.

RESULTS

A total of 1199 responses were obtained from the University College of Medicine (n=355), University College of Dentistry (n=195) and Institute of Allied Health Sciences (n=649). Of these 159 respondents were faculty members, while 1040 were students. The age of the participants was between 18 and 60 years however, most of the respondents were female and from age range of 18-37 years. (Table I).

Table 2 shows the stress levels among students and faculty based on their institution and gender. Students from University College of Medicine reported higher score on the perceived stress scale (23.02$\pm$11.85) than those from University College of Dentistry (21.87 $\pm$ 10.86) and Institute of Allied Health Sciences (21.95 $\pm$ 11.32). A higher stress level was reported among faculty of University College of Dentistry (18.71 $\pm$ 9.99). The differences among cumulative scores of the institutes was not significant. However, the medical students did report significantly higher scores on various items of the PSS-10 scale. The mean scores of students and faculty on all items suggests that they had experienced stress 'sometimes to fairly often' during this pandemic. Their scores on all items and subsequently, the stress level was significantly higher than the faculty. Females experienced more stress than males and these differences were significant for all the items among faculty. There were no significant differences among students and faculty of various age groups indicating a similar impact of the pandemic on all age groups.

DISCUSSION

The students and the faculty from medicine, dentistry and allied health sciences institutes had moderate stress levels during COVID-19 pandemic. The finding that females experienced significantly more stress than males during the on-going pandemic is in line with the previously conducted studies across European countries [8,9]. A Chinese study conducted during the peak of this pandemic also reported that females were more vulnerable in developing anxiety and depression as a result of being exposed to constant stress. It has been reported that all health professionals, irrespective of gender, are stressed and anxious as they are struggling to strike a balance between teaching and providing healthcare, while ensuring their own safety as well as of their families [3]. There is a need for equity-based policies to control stress and anxiety among females.

The stress levels were higher amongst students in comparison to the faculty. The students reported being unable to control the important things in their lives. This is consistent with findings in literature, as students have reported to find the situation 'unnerving' [10]. The uncertainty of the situation and the question as to when life will go back to normal may have also led to increased levels of anxiety amongst students. Such stress has a negative impact on the mental well-being and in turn the learning capabilities of students [11]. The stress levels may have been aggravated by the transition from face to face towards online teaching and learning. With online teaching and learning, students have reported limited attention spans and increased cognitive load [6]. Many have also identified e-learning to be resource intensive and not all students have access to good quality gadgets and high speed In-

Table 1: Age-wise distribution of ED patients in both Groups (200)

	Type	University College of Medicine	University College of Dentistry	Allied Health Sciences	P value		
		Mean+ SD	Mean+ SD	Mean+ SD	UCM vs UCD vs AHS	Faculty vs Students	Male vs Female
1. In the last month, how often have you been upset because of something that happened unexpectedly?	Students	2.46+1.12	2.48+1.15	2.55+1.10	0.537	0.024*	0.007*
	Faculty	2.29+0.99	2.47+1.00	2.35+1.00	0.66		0.002*
2. In the last month, how often have you felt that you were unable to control the important things in your life?	Students	2.39+1.14	2.36+1.09	2.36+1.21	0.86	0.0002*	0.007*
	Faculty	1.84+1.17	2.37+1.15	1.85+1.16	0.12		0.00*
3. In the last month, how often have you felt nervous and stressed?	Students	1.11+2.64	1.19+2.44	1.17+2.59	0.256	0.000*	0.005*
	Faculty	0.88+2.33	1.18+2.33	0.98+2.00	0.15		0.0001*
4. In the last month, how often have you felt unconfident about your ability to handle your personal problems? (+)	Students	1.07+1.62	0.99+1.36	1.02+1.54	0.02*	0.0004*	0.120
	Faculty	0.72+1.00	0.92+1.20	0.98+1.10	0.61		0.00*
5. In the last month, how often have you felt that things were not going your way? (+)	Students	1.10+2.23	1.13+2.18	1.12+2.13	0.29	0.0005*	0.53
	Faculty	0.92+1.58	0.99+1.67	0.91+1.68	0.87		0.006*
6. In the last month, how often have you found that you could not cope with all the things that you had to do?	Students	1.69+2.40	1.05+2.09	1.07+2.11	0.001*	0.002*	0.051
	Faculty	1.00+1.91	1.08+2.17	0.83+1.78	0.28		0.0003*
7. In the last month, how often have you been unable to control irritations in your life? (+)	Students	1.06+2.12	1.06+1.85	1.10+1.81	0.0003*	0.00*	0.166
	Faculty	0.82+1.29	0.99+1.33	1.19+1.60	0.49		0.004*
8. In the last month, how often have you felt that you were not on top of things? (+)	Students	1.14+2.39	1.01+2.36	1.13+2.13	0.006*	0.002*	0.379
	Faculty	1.05+1.98	0.93+1.87	0.90+2.05	0.79		0.026*
9. In the last month, how often have you been angered because of things that happened that were outside of your control?	Students	1.16+2.44	1.04+2.42	1.18+2.49	0.58	0.0001*	0.042*
	Faculty	1.09+2.01	0.86+1.87	1.08+2.00	0.82		0.00*
10. In the last month, how often have you felt difficulties were piling up so high that you could not overcome them?	Students	1.26+2.33	1.15+2.33	1.21+2.24	0.433	0.0007*	0.090
	Faculty	1.22+1.85	0.89+1.43	1.10+1.63	0.22		0.0001*
Total	Students	11.85+23.02	10.86+21.87	31 11+21.95	0.29	0.002*	0.13
	Faculty	9.86+18.08	9.99+18.71	10.13+18.04	0.50		0.003

* The differences are significant ($p<0.05$). + Four statements were originally positive, therefore reversed.

ternet [6]. This is alarming as perceived stress is shown to have a strong positive correlation with fatigue, depression and procrastination [9].

The results of our study highlighted that medical students experienced higher stress than the dental and allied health students. This is consistent with findings from literature, which states the mental health of medical students to be poorer in comparison with other students[12]. A global study that was conducted to assess the mental health of medical students also concluded that medical students show high levels of mental stress and depression and are hence most likely to resort to substance abuse as a coping strategy [13]. Academic stress is a major factor that contributes towards the increased stress levels of medical students. This stress coupled with the on-going pandemic, lack of on-campus activities and peer interaction may have further aggravated the situation [14].

As stress levels have been determined and the most stressed subpopulations has been identified, the findings of this study can assist administrators in chalking a plan of action for looking after the mental health of students and faculty. In light of the insight gained by this study, the institutions should assess mental health and provide for necessary services to the students. The first step can be holding open discussions on mental health to remove the stigma around it. Allowing flexible study

or work schedules, so neither the students nor faculty feels overwhelmed by the workload. Additionally, online counselling sessions, workshops on coping and stress management such as through mindfulness-based stress reduction exercises may also be useful. Taking timely corrective measures is imperative to maintain the psychological wellbeing of both students and faculty members. It is important to highlight that stress and mental health are still stigmatized in the country and further research needs to be undertaken to identify the most suitable modality for ensuring emotional wellbeing of students and the faculty.

We could not find any studies that used PSS-10 scale to measure stress among students and the faculty during the pandemic, therefore comparison of all aspects of the results was not possible. All the medical, dental and allied health science institutions were affiliated by a single university from Lahore, Pakistan. Therefore, similar studies are needed from institutions in other provinces of Pakistan.

CONCLUSION

During COVID-19 pandemic, the students and the faculty from the medicine, dentistry and allied health sciences institutes were moderately stressed. The pandemic had a significant impact on all the age groups. The medical students were more affected than the allied health students and the faculty. Likewise, the females were in more distress than males. Institutions should hence promote resilience by offering support services to manage mental health conditions. Future studies should explore the lived experiences of the students during pandemic qualitatively.

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Zaidi SHR:	Acquisition and critical review
Arooj M:	Analysis and interpretation of data
Sethi A:	Concept, Design, Final approval

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

ORIGINAL ARTICLE

DETERMINATION OF FOOD PRESERVATIVES (BENZOIC AND SORBIC ACIDS) IN BAKERY PRODUCTS OF DISTRICT PESHAWAR, PAKISTAN

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ABSTRACT

Objective: To determine the level of preservatives (Benzoic and Sorbic acid) in bakery products of Peshawar

Material and methods: This cross-sectional study was performed in district Peshawar from August 2019 to December 2019 by visiting four bakery stores in each union council (total of ten union councils) by collecting three samples (of biscuits, cakes and bread) from each bakery stores using multistage convenient sampling technique. Thus, a total of 120 samples were collected. Food additives in the form of Benzoic and Sorbic acid were checked in Forensic and toxicology laboratory of Khyber medical college Peshawar. Data was analyzed using SPSS 23, where frequencies and percentages were used for categorical variables and mean. Standard deviation for numerical data.

Results: In samples of cakes, concentration of benzoic acid (BA) ranged from 314 to 457 ppm (WHO permissible limit is up to 500ppm) while that of sorbic acid(SA) ranged from 597 to 859 ppm (WHO permissible limit is up to 1000ppm). Similarly, concentration of benzoic acid in biscuits samples ranged from 363 to 467 ppm and sorbic acid ranged from 649 to 895 ppm. In bread samples, BA ranged from 350 - 487 ppm and sorbic acid ranged from 619 to 944. Comparing the values with WHO standards for preservatives, the concentration of benzoic and sorbic acid is found to be within permissible limits with p value < 0.05.

Conclusion: Benzoic acid and Sorbic acid were found in permissible limits in 3 bakery products in the city of Peshawar, as set by World Health Organization.

Keywords: Bakery products, Additives, Preservatives, Bakeries

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INTRODUCTION

When we have to store food for a prolonged period, additives are added to maintain the quality and the taste. These additives stop bacteria and fungus from growing by removing additional water[1]. Preservation of food is one of the oldest methods used by people that can inhibit changes which occur due to action of microbes, enzymes and physical agents[2,3]. A preservative can be natural or synthetic, which we add to food to prevent deterioration by bacteria or atmospheric effects. Chemical preservatives such as Sulphur dioxide, sorbic acid, propionic acid and sodium benzoate are increasingly used by the baking industry mainly because of high demand for good quality, safe and fresh food[4,5]. Preservatives when added to food minimize food wastage which can be caused by microbes. In this way these can be stored in stores and homes for longer period[6].

Bakery Products have an important place in food consumption[7]. Commonly consumed bakery products are bread, biscuits and cakes which make up to 80% of the products produced in most of the countries[8]. Changing life styles and dietary habits have resulted in increased demand of ready to eat food[9]. Foods in which preservatives are used because of their antimicrobial activity are cakes, butter, pie and doughnuts[10]. Studies have proven that on an average, every individual can annually consume up to 3 to 5 kg or even higher quantity of food additives[11]. Additives are mostly added to all forms of food, ranging from the less processed to the highly processed ones[12].

The association between added chemicals and the health is not a good one. In the 1980s, food chemicals were thought to be harmful to be used by humans, which resulted in fear of using them, and some of them were excluded from list. Later, it was proven by different studies that not

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all of them were harmful, although there were doubts about the effects of these on health[13]. Like any other medicinal chemical, preservatives can initiate hazardous reactions like allergic reactions and even carcinogenesis[14]. Many studies have shown that particular levels of artificial preservatives and their long-term use can cause carcinogenicity and genotoxicity[15,16]. Recent research is encouraging the use of agents that are natural and have got antimicrobial activity to replace the commonly used synthetic preservatives thus reducing their hazardous impact over health[17]. While in Pakistan, the quality control measures are inadequate, studies to estimate the levels of food preservatives are not yet conducted at all in our province. This study will highlight the level of food preservatives that will help food control authority to regulate the quality and standards of bakery products in the district Peshawar.

MATERIAL AND METHODS

This cross-sectional study was performed in the district Peshawar from August 2019 to December 2019 by visiting four bakery stores in each union council, in a total of ten union councils by collecting three samples of (biscuits, cakes and bread) from each bakery store using multistage convenient sampling technique. Thus, a total of 120 samples were collected. Sample size was calculated using WHO sample size calculator, using Prevalence of 93% of benzoic acid found in bakery products in study conducted in Iran[18]. After collection of samples, the analysis was done by High Performance Liquid Chromatography in Forensic and toxicology laboratory of Khyber Medical College Peshawar.

RESULTS

In samples of cakes, concentration of benzoic acid (BA) ranged from 314 to 457 ppm (WHO permissible limit is up to 500ppm) while that of sorbic acid(SA) ranged from 597 to 859 ppm (WHO permissible limit is up to 1000ppm). Similarly, concentration of benzoic acid in biscuits samples ranged from 363 to 467 ppm and sorbic acid ranged from 649 to 895 ppm. In bread samples, BA ranged from 350 - 487 ppm and sorbic acid ranged from 619 to 944. Comparing the values with WHO standards for preservatives, the concentration of benzoic and sorbic acid is found to be within permissible limits with p value < 0.05. See table 1-6 for details. Fig-1 shows level of benzoic and Sorbic acids in three food products.

DISCUSSION

The results of this study revealed that preservatives are present in all bakery products and they are found to be

Table 1: Frequency of different types of bakery products

Types of bakery product	Product No	Percentage
Bread	40	33.3%
Biscuit	40	33.3%
Cake/Pastery	40	33.3%
Total	120	100.0%

Table 2: Comparison of Food preservatives (BA & SA) in Cakes in Different Union Councils

UCs	Benzoic acid: Mean & (S D)	Sorbic acid: Mean (SD)
UC 1	449.25(8.18)	836.75(45.828)
UC 2	455.00(8.446)	859.50(55.842)
UC 3	451.50(22.487)	789.50(173.09)
UC 4	454.50(25.736)	811.25(50.566)
UC 5	419.75(49.149)	852.00(141.393)
UC 6	457.75(75.522)	663.25(59.011)
UC 7	389.50(74.942)	597.00(141.353)
UC 8	374.25(67.342)	759.75(74.437)
UC 9	390.75(76.443)	728.25(186.382)
UC 10	314.00(60.619)	612.25(33.180)

Table 3: Comparison of Food Preservatives (SA&BA) in Bread in different Union Councils

UCs	Benzoic acid mean & (SD)	Sorbic acid mean & (SD)
UC 1	487.75(29.159)	812.00(59.121)
UC 2	472.00(26.633)	813.50(47.007)
UC 3	461.00(40.042)	825.50(110.147)
UC 4	409.50(60.341)	944.25(34.121)
UC 5	400.25(15.064)	807.25(116.554)
UC 6	376.75(107.398)	697.00(146.592)
UC 7	350.00(87.939)	827.75(69.687)
UC 8	380.75(105.844)	619.50(114.684)
UC 9	404.25(92.330)	727.00(171.587)
UC 10	373.50(101.773)	872.50(94.296)

Table 4: Comparison of Preservatives (BA &SA) in Biscuits in different Union councils

UCs	Benzoic acid mean & (SD)	Sorbic acid mean & (SD)
UC 1	458.75(45.683)	886.00(25.073)
UC 2	460.75(13.276)	889.50(90.780)
UC 3	467.25(24.245)	753.00(42.591)
UC 4	450.25(51.803)	721.50(183.945)
UC 5	436.50(48.446)	841.50(116.119)
UC 6	364.00(93.192)	701.50(72.247)
UC 7	376.50(32.808)	895.75(93.870
UC 8	403.50(32.563)	829.25(93.870)
UC 9	394.75(128.181)	649.75(150.050)
UC 10	363.75(68.070)	815.00(179.907)

Table 5: Comparison of Benzoic acid with FDA criteria applying (one sample T test)

Level of BA in biscuits	Test value	T test	DF	sig	Mean Difference	95% C.I	
						Lower	Upper
	500	-21.600	39	0.001	-260.40	-284.78	-236.01
Level of BA in cake	1000	-75.24	39	.0001	-683.87	-702.25	-665.49
Level of BA in bread	500	14.59	39	.0001	294.62	253.79	335.45

P value = 0.0001

Table 6: Comparison of Sorbic acid levels with FDA criteria (one sample t-test)

SA in biscuits	Test value	T test	DF	sig	Mean Difference	95% C.I	
						Lower	Upper
	500	9.73	39	0.0001	-201.72	-243.6	-159.7
SA in cake	1000	-58.5	39	0.0001	-124.05	-129.2	-1205.8
SA in bread	500	14.59	39	0.0001	294.62	253.79	335.45

P value = 0.0001

CI is also significant

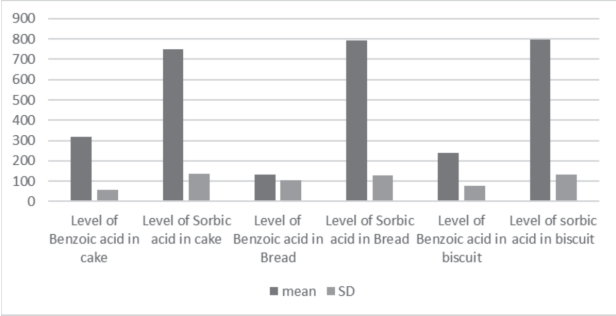

Fig 1: Comparison of Benzoic and Sorbic Acid in three food products

within permissible limits set by WHO. Intake of food exceeding the minimum permissible carries a definite health risk, but at the same time these risks carry a strong association with level of consumption and accurate calculation of these additives. Studies have shown that safe food practices result in healthy population which improves the economic growth of those countries. WHO has set certain standards for food additives so that they cause less toxicity because it is proven that food additives cause genetic mutations if consumed in large amounts[19]. Different countries either use the WHO criteria for preservative addition or set their own standards which is consistent the findings of this study where in Pakistan WHO set standards are followed[20]. The addition of natural ingredients to bakery products in our study is consistent with the practice in developed countries where demand for "clean label" is being introduced and people of the bakery industry are deviating from using chemicals as food additives[21]. Studies carried out in most of the countries show that Benzoic acid and Sorbic acid are frequently used preservatives either alone or together. In our study, sorbic acid and benzoic acid levels in cake samples are found mixed together within the range of 595-859 ppm and 314-457 ppm respectively. A study conducted in Egypt by Mahmoud Gamal reported that the levels of Sorbic acid in cake were 288-659 ppm while benzoic acid was not detected. These findings are not consistent with our study which shows that both the preservatives are present together[22]. A study in Iran reported the levels of benzoic acid were from 350 to 1520 ppm while sorbic acid was found to be from 850 to 2300 ppm in bread samples. The results showed that benzoic acid and sorbic acid widely occur in food products in Iran. This study results also show that great variation is found in preservative added to food from country to country & region to region, so the associated health risks also differ[23]. Samples in case of Iran show no benzoic acid at all. Another finding which was not consistent with the results of our study was detection of both these additives in bread sample. Again, the levels were lower in samples of Iran and benzoic acid was not detected in their samples. This also shows that different countries use their own criteria at times[24].

The results of our study show that level of benzoic acid and Sorbic acid in cake differ from cake samples checked in Yemen and Iran where the study showed that the levels of these preservatives was found to be lower, while samples in case of Iran show no benzoic acid at all. Another finding which was not consistent with the results of our study was detection of both these additives in bread sample [25].

This study has limitations in many respects, the samples are taken from one city where public health regulations are adopted stringently. Sample collection from areas out of main cities might show variations in preservatives use. Another limitation of this study is the fact that we selected only three bakery products.

CONCLUSION

Benzoic acid & Sorbic acid were found in permissible limits in these bakery products, as set by World Health Organization. Large sample size including multiple products

and venues in far flung areas are needed to estimate the true magnitude of preservatives addition in food products.

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AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under

Mustafa A:	Helped in literature review, data analysis and writeup.
Ayub R:	Conceived study, collected data and did literature review and data analysis.
Irfan S:	literature review and Writeup.
Iftikhar B:	Data analysis, critical review, overall supervision
Inamullah M:	Bibilography

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

ORIGINAL ARTICLE

ORAL HEALTH-RELATED QUALITY OF LIFE AND ITS ASSOCIATED FACTORS IN ELDERLY POPULATION

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ABSTRACT

Objectives: This study was aimed to evaluate oral health-related quality of life and its associated factors in the elderly.

Material and Methods: A cross-sectional study was done at the medical Out Patient Department of Khyber Teaching Hospital Peshawar by using a non-probability consecutive sampling method of 411 elderly patients. All the patients had an oral examination, followed by an interview through a validated questionnaire having demographics and oral health-related quality of life (OHRQoL) was measured using OHIP-14 having Likert scale, with higher scores indicating poor oral health (lower OHRQoL) and vice versa. Results: The mean OHIP-14 score (range 0-56) was 62.35± 10.94 which is much higher than the threshold for poor OHRQoL 'poor OH' ≥11.0 (SD ± 6.9). OHRQoL was found good in the participants having good oral Hygiene (51.74) and who were more qualified. Females had relatively good OHRQoL (61.4). The mean OHIP score was higher in the participants belonging to rural areas (67.1) as compared to urban areas.

Conclusion: This study found poor OHRQoL in the elderly population in Peshawar. Participants who had good oral hygiene & who were qualified had good OHRQoL. OHRQoL was found poor in rural areas participants; it was relatively good in females as compared to males.

Keywords: Elderly population, Oral Health-Related Quality of Life, Oral Hygiene, Oral Health Impact Profile.

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INTRODUCTION

The expansion of the definition of health by WHO led to the concept of wellbeing and wellbeing is measured by improvement in quality of life[1,2].

As the oral health-related quality of life is a multi-dimensional thought, which deals with dental health and its impact upon wellbeing, therefore, it is difficult to assess OHRQoL. Research groups have made considerable efforts to develop a tool for the measurement of the impact of impairment on life. Most of the instruments concentrate on problems in the oral cavity and some of them assess the positive effects of oral condition on OHRQoL[3,4,5].

The oral health impact profile is the questionnaire that is mostly used for measuring Oral health-related quality of life. This Questionnaire quantifies the impact of oral issues and covers physical, psychological, and social dimensions of daily routine. Its original version had 49 items later on it was changed to OHIP-14, it is so named because it has 14 dominions. This shortened form of OHIP-14 had equal sensitivity to the old version which had 49 items It is divided into seven domains having two questions in each domain. These seven domains are (functional limitation, physical pain, psychological discomfort, physical disability, psychological disability, social disability, and handicap). The responses are scored on a Likert scale having five points which are from never to very often. OHIP-14 has been used in the Pakistani population by Ibrahim Warsi et al in Karachi[6,7].

There is a paucity of research in this province on the effect of oral hygiene status, education level, gender, and address on OHRQoL. The objective of the present research was to find the relation of OHRQoL with oral hygiene, qualification, gender, and address.

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MATERIAL AND METHODS

This research was carried out to measure oral health and its related quality of life in the older population coming to Khyber Teaching Hospital (KTH), Peshawar. Research data was collected in the outpatients' department of the Department of medicine of Khyber Teaching hospital over

three months using a non-probability consecutive sampling technique. All patients above the age of 60 years, visiting the medical outpatient department of the MTI KTH for seeking treatment of their clinical diseases were recruited in the study. Patients with serious clinical issues including blood disorders, physically and intellectually debilitating conditions were excluded. Research data was collected after the informed consent of the participants. Taking population proportion of 50%, a margin of error of 0.05, and power of study 80% in WHO sample size calculator the calculated sample size was 385, while 411 participants were easily included in the study.

After the ethical approval for the research and informed written consent, the patients had oral examination using a disposable spatula and convenient light. After having the oral examination, all the participants were asked questions in the questionnaire having demographics and OHIP-14 used for measuring oral health-related quality of life.

The questionnaire of OHIP-14 is divided into seven domains with each domain having two questions. These seven domains are (functional limitation, physical pain, psychological discomfort, physical disability, psychological disability, social disability, and handicap).

The answers of the participants were scored on a Likert scale having five points which are from never to very often. The range of the OHIP-14 scale is 0 to 56 where greater scores show poor OHRQoL and lower score shows good OHRQoL. The standard value for 'good oral health is $\leq 9.33 \pm 6.5$ and for poor Oral hygiene is $\geq 11.0 \pm 6.9$. Overall Visual Oral Hygiene was defined as apparently generally visualized by the observer.

Data was entered and analysis was performed on SPSS version 21, keeping the confidence interval at 95% and α value at 0.05. Analysis of descriptive variables was done and a t-test was performed for mean comparison OHIP score in two groups. ANOVA was used to compare the mean OHIP score between more than two groups.

RESULTS

Out of the total 411 participants, the mean age was 67.79± 5.3 with an age range from 60-80 years of age. The mean OHIP Score (range 0-56) of this study was calculated as 62.35 SD ± 10.940 and this is greater than the value for bad OHRQoL, which is OHIP-14 score greater than 11 ±6.5, by applying one-sample t-test t value was greater 91.23 p-values .000 thus showing a greater difference between the mean score of this study and standard value which is 11.

This table shows that majority were reported as "quite often" having had problems in the last one year on 10 of the 14 items (ranging from Experience of disturb sleep (41.6), avoid smiling (42.67), food getting stuck (45.3), avoid eating a certain food (47.2), feeling less confident (49.1), the experience of bad breath (51.6), experience discomfort eating (53.8), spending a lot of money on dental problems (57.9), experience shyness (59.6) and experience of ulcers (60.6). There were relatively fewer participants who reported that they "sometimes" had problems of disturbed concentration (40.1) & avoid going out (41.6). Regarding the variable of overall visual oral hygiene applicants with good oral hygiene had a good oral health-related quality of life followed by those with fair oral hygiene and those who had poor oral hygiene had poor oral health related quality of life (Table. 4).

On account of the variable of the level of education those participants who were illiterate, had a high mean OHIP score (64), followed by primary (61.68), matric (61.58), and intermediate (59.11), while those participants who were graduates had a lesser score of 47.15. Hence this study shows that as the level of education increases the mean OHIP score decreases and the quality of life gets better (Table. 4).

By applying the Independent Sample T-test it was found that the male participants had relatively higher OHIP score i.e. 62.7±10.36, as compared to the female with 61.4±12.08 with a p-value of 0.235, thus females had a relatively good oral health-related quality of life as compared to males (Table 4) and this was statistically significant. According to the variable of address, the mean OHIP score was higher i.e. 67 in participants belonging to rural areas as compared to urban areas which were 58, which means the oral health-related quality of life was good in the urban participant as compared to rural participants (table-4). Table 4: Distribution of visual oral hygiene, educational level, and gender with OHIP score

Table 1: Baseline Characteristics of the participants

Baseline Characteristics	Categories	Frequency	Total Frequency	%age
Age in years	69 – 60	250	411	60.8
	80 – 70	161		39.2
Gender	Male	256	411	62.3
	Female	155		37.7
Address	Rural	188	411	45.7
	Urban	223		

Table 2: One-Sample Statistics

OHIP score of the applicant				
N	Mean	SD	S.E. Mean	P-Value
409	62.35	10.940	0.541	0.005

Table 3: Description of the Answers to OHIP-14

Distribution of OHIP items ranging from 0 (never) 1 (seldom) 2 (sometimes) 3 (quite often) 4 (very often)								
Description of items		Distribution of responses (%) n						
Items	Questions	0	1	2	3	4	Mean	S.E.
Functional Limitations								
OH – 1	Chewing difficulty	(5.4) 22	(10.5) 43	(25.1)103	48.9(201)	10.2(42)	2.48	0.49
OH – 2	Bad breath	(7.8) 32	(13.1) 54	(20.4) 84	(51.6) 212	(7.1) 29	2.37	0.052
Physical Pain								
OH – 3	Discomfort eating	(3.2) 13	(10.7) 44	(23.4) 96	(53.8) 22	(19) 37	2.55	0.045
OH – 4	Ulcers	(4.6) 19	(11.7) 48	(11.4) 47	(60.6) 249	(11.7) 48	2.63	0.048
Psychological Discomfort								
OH – 5	Food getting stuck	(5.4) 22	(5.6) 23	(32.8) 135	(45.3) 186	(10.9) 45	2.51	0.047
OH – 6	Feeling shy	(2.2) 9	(9.7) 40	(17.5) 72	(59.6) 245	(80.9) 45	2.67	0.043
Physical Disability								
OH – 7	Avoid eating	(5.4) 22	(8.8) 36	(27.5) 113	(47.2) 194	(11.2) 46	2.50	0.049
OH – 8	Avoid smiling	(7.5) 31	(0.7) 44	(28.7) 118	(42.6) 175	(10.5) 43	2.38	0.052
Psychological Disability								
OH – 9	Disturbed sleep	(8.3) 34	(12.2) 50	(27.3) 112	(41.6) 171	(10.5) 43	2.35	0.054
OH – 10	Disturbed concentration	(3.9) 16	(9.7) 40	(40.1) 165	(36.0) 148	(10.2) 42	2.39	0.046
Social Disability								
OH – 11	Avoid going out	(8.6) 27	(31.6) 13	(41.6) 171	(10.2) 42	(10) 44	1.85	0.051
OH – 12	Less confident	(5.1) 21	(10) 41	(26.3) 108	(49.1) 202	(19.5) 39	2.48	0.048
Handicap								
OH – 13	Daily activities affected	(5.1) 21	(10.9) 45	(43.1) 177	(32.4) 133	(8.5) 35	2.28	0.047
OH – 14	Increase expenditure on dental problems	(7.3) 30	(9.0) 37	(15.1) 62	(57.9) 236	(11.1) 46	2.57	0.052

Table 4: Distribution of visual oral hygiene, educational level, and gender with OHIP score

		N	Mean	S.D	P-Value
Visual oral hygiene	Good	53	51.74	9.340	<.005
	Fair	83	52.81	8.812	
	Poor	275	67.11	8.408	
Levels of Education	Illiterate	183	64.38	8.471	<.005
	Primary	124	61.68	12.619	
	SSC	64	61.58	13.888	
	HSSC	27	59.11	5.423	
	Bachelors & above	13	47.15	5.273	
Gender of the participants	Male	256	62.74	10.360	.235
	Female	155	61.41	12.084	
Address of the participants	Rural	188	67.1	8.521	<.005
	Urban	223	58	8.201	

DISCUSSION

The mean OHIP score in the present study was greater than 11 ± 6.5 which is the cut-off value for bad oral health, thus showing a greater difference between the mean score of this study and the standard value which is 11. This means that the oral health-related quality of life of the participants was found poor. Similar findings were found in the study done by Warsi et al[7] where the OHIP score was 23.38± 10.47 i.e. oral health-related quality of life was also poor. The findings of Kim et al, on the other hand, contradict the findings of the present study in which the mean OHIP-score was 10.66 ±10.7 which is in the range of good oral health-related quality of life[8]. In a study done by Young et all in 2009 in Korean elders, the median OHIP score was 7, which was also in the range of good oral health related quality of life[9].

Participants having good oral hygiene had a good oral health-related quality of life, these findings are in line with the findings of Kung Hee Lee 2013 in west Virginia those participants who had lower OHIP scores also had good oral hygiene[10].

Illiterate participants had high OHIP scores i.e. poor oral health-related quality of life as compared to educated participants. The same findings were reported by Kari Elisabeth 2010 in which individuals with higher education had a good oral health-related quality of life[11]. The present results are in line with those of previous studies and confirm that level of education is associated with oral health-related quality of life Ekback et al [12].

In our study, there was a statistically insignificant (p-value= 0.23) association between gender and the OHIP score of the participants. These findings contradict the results of Kari Elisabeth Dahl in 2011 in which women reported poorer oral health-related quality of life as compared to the males participants[13]. Einarson et al also reported the same findings in their study in 2009 that females have a poor oral health-related quality of life relatively to males and likewise same findings were found in the study of Inukai et al in 2010 in which oral health-related quality of life was good in males (correlation coefficient -0.60) as compared to females (-0.46)[14,15]. The findings of Kim et all study in 2009 are however in agreement with the results of the present study, that male participants had a higher mean OHIP score (12.2 SD 11.0) as compared to females (9.8 SD 10.5)[8]. Factors responsible for the better oral health of females is that they are more conscious about their health and fitness.

Participants from the urban area had a good oral health-related quality of life as compared to rural areas. These findings are similar to the results of McGrath C, John MT, Mesalu JR in which OHRQoL is found good in urban areas, which might be because rural people have much less access to the health services which lead to late treatment [16,17,18].

LIMITATION OF THE STUDY

One limitation of our study is that it was carried out in a hospital setting which is not ideal; it however provides baseline data over which further research can be done for finding the actual Oral health-related quality of life mean value in a community setting.

CONCLUSION

According to this research Oral health-related quality of life was found poor in geriatrics and confirms that oral health also has impacts on other aspects of life. Those who had a positive attitude towards oral health had a good quality of life.

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AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under

Liaquat S:	Idea and conceptualization, manuscript writing, final critical review and appraisal
Khan A:	Planning, manuscript writing, formatting and critical review
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Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

ORIGINAL ARTICLE

THE RATE OF SUCCESS IN UTEROVAGINAL PACKING IN ATONIC UTERUS IN A TERTIARY CARE HOSPITAL IN LOW RESOURCE SETTING

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ABSTRACT

Objective: To find out the success rate of Uterovaginal packing of Atonic Uterus in a tertiary care hospital, in low resource setting.

Methods: This was a cross-sectional study conducted in Gynaecology and Obstetrics department of Lady Reading Hospital from January 2019 to December 2019. Our study included those patients with PPH not responding to medical treatment in vaginal delivery. Patients in shock with PPH and PPH after Caesarian section were excluded from the study. The study was approved by the ethical committee of hospital.

Results: In our study 250 patients with Atonic Uterus were subjected to uterovaginal packing after medical treatment failed in these patients. The success rate after 12 hours was 86.4%. In rest of the patients, PPH was controlled by second line surgical intervention in 34 cases (13.6%), B Lynch in 18 (7.2%) cases, subtotal hysterectomies in 13 (5.2%) cases and internal Iliac ligation in 3 cases (1.2%)

Conclusion: Uterovaginal packing is an effective, easy, quick and lifesaving method in the control of PPH in low resource settings.

Key Words: Primary postpartum hemorrhage, Internal Iliac Ligation, Retained products of conception(RPOCs)

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INTRODUCTION

Worldwide, 5 million maternal deaths occur annually, out of which, 150,000 are due to PPH.[1] In developing countries, the risk of maternal deaths from PPH is 1 in 1000 deliveries.[2,3] Moreover, PPH may result in serious morbidities like coagulopathy and renal shutdown. Uterine Atony is the leading cause of PPH in more than 90% of cases.[4] In these cases, uterotonics are given and if not effective, then before proceeding to operative procedures like B lynch, internal iliac ligation and hysterectomies, an alternative and more conservative procedure of Uterovaginal packing can be applied. [5, 6] It compresses the uterine sinuses by pressure effect just like Balloon Tamponade and hence controls bleeding by quick and cheap way in a low resource setting. In most cases bleeding stops and patient is saved from invasive procedures. In other cases, patient is stabilized while preparing for surgery and sometimes surgery is not needed as the bleeding gets stopped with this conservative procedure.[7,8]

We conducted this study to see the success of this procedure in low resource settings having a high rate of PPH. No studies have been conducted on this procedure in the recent years despite the fact that it is being frequently used to control PPH in tertiary care hospitals.

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MATERIALS AND METHODS

This was a cross-sectional study conducted in Lady Reading Hospital Peshawar from January 2019 to December 2019. Patients with PPH with Atonic uterus were included in the study. Those in shock due to PPH, PPH after C section, secondary PPH, RPOCs and genital tract trauma were excluded from the study. The sample size of 250 was calculated by WHO sample size calculator by taking the prevalence of PPH in pregnancy as 7%, confidence interval 95% and margin of error as 5%. The study was approved by ethical committee of the hospital. After informed consent, patients were included the study, and a detailed history and clinical examination was done.

Under good light, Sims speculum was passed with cervix held with Volsellum. A 6-meter sterilized gauze was passed layer by layer starting from fundus occupying the whole uterine cavity till the cervix. Further, this packing was

extended into the vagina to add pressure and good compression to the uterus. Prophylactic single dose antibiotic was given, the pack was kept for 12 hours and Syntocinon infusion was continued for 6 hours. Patients were kept in High Dependency Unit with strict vital record. Patient were declared stable after 12 hours without any untoward events. Data of these patients was analyzed using the SPSS version 23.

RESULTS

A total of 413 patients of PPH presented to the unit in this study period, out of which 250 patients with Atonic uterus underwent uterovaginal packing. The maternal age was 34.6±4.68, Gestational age was 36.2±1.65 and Parity was 6.08±1.64 (as shown in Table 1).

The success rate of uterovaginal packing after 12 hours was 86.4% as given in Table 2 and 13.6% needed second line surgical intervention as can be seen in Table 3. Subtotal hysterectomy was performed in 13 patients (5.2%), B Lynch was done in 18 cases (7.2%), and Internal iliac ligation was done in 3 patients (1.2%). Mortality of these patients in the study period was found to be zero.

Table 1: No of patients coming with PPH (n=413)

Causes of PPH	Number of patients	Frequencies
Atonic Uterus	250	%60.53
Genital Tract Trauma	43	%10.72
RPOCs	61	%14.76
Retained Placenta	47	%11.38
Coagulopathy	12	%2.90

Table 2: Demographic features of patients with PPH

Variables	Mean
Maternal age	4.68±34.6
Gestational age	1.65±36.2
Parity	1.64±6.08

Table 3: Success Rate of Uterovaginal Packing (n=250 Patients)

Procedure	No of patients	Frequency
Uterovaginal packing	226	%86.4
Second line surgical intervention	34	%13.6

DISCUSSION

PPH is a major cause of maternal morbidity and mortality. Uterovaginal packing was used to control PPH in 1960s, but due to the risk of infection, its use declined. But in 1990s, its use again started to gain popularity. [9] This modality is most useful in controlling bleeding due to Atonic uterus not responding to medical treatment and placenta previa and accreta.[6] Uterine packing has been recommended by Begga et al. to control bleeding in cases of uterine atony not responding to medical treatment [9].

In the present study the success rate of controlling the bleeding was 86.4% which was comparable to studies done by Bagga R, 84.7 % by Pradhan B et al, 86% by Haq et al, , 86% by Bhatti K et al, 91.8% by Singh P et al. [9,10.12,13,14] In the study done by Ali et al. on uterovaginal packing in 46 (86%) patients with PPH, 14 patients failed to achieve haemostasis with 6 (14%) patients having caesarean hysterectomy, internal iliac ligation in 3 (7%) patients, 4 patients had b Lynch, 1 (2%) died and 13 patients had multiorgan failure. These results were comparable to our results in success and second line invasive procedures used were the same.[15] Uterine gauze packing is also effective in cases of bleeding from placental bed in cases of placenta accreta by Shao et al.[16]

In studies done by Haq et al and Nwagha et al. reported uterovaginal packing as 12-24 hours according to the cases. In our study, we kept the pack for 12 hours while monitoring the vitals and increase in fundal height.[12,17]

Our study results were comparable to a 4 years' observational study in low resource setting in which Foley's catheter had a 53% efficacy in controlling PPH and the uterovaginal packing had a much higher efficacy of 93%. Second line surgical intervention is the only option in patients with PPH to control the bleeding in which conservative management fails. In our study, 34 patients (13.6%) underwent surgical intervention which were comparable to surgical intervention for PPH done in other study done by Iram et al.[18]

In developing countries, 70% of patients are delivered without skilled birth attendants and there are no facilities and expertise available for advanced procedures like pelvic devasculirization and balloon tamponade. In such circumstances, uterovaginal packing is a good substitute for tamponade and can be done by less trained birth attendant to control bleeding and in the meanwhile, referring patient to a tertiary care hospital, because time is of prime importance in cases of PPH to save the life of a patient.

Limitations of this study include, small sample size and single center experience. Further large scale studies are required to compare Uterovaginal packing with balloon tamponade.

CONCLUSION

Uterovaginal packing is a quick, economical and effective procedure in controlling bleeding in PPH in hemodynamically stable patients and can be done by a less expert medical personnel in a low resource setting.

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AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under

Sabir SA: Idea, Proposal Writting, Data collection, Writting.

Sultan S: Data collection, Writting.

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

ORIGINAL ARTICLE

THE SAFETY OF VEROCELL COVID -19 (SINOPHARM) VACCINATION AMONG HEALTH CARE WORKERS IN KHYBER TEACHING HOSPITAL, PESHAWAR

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ABSTRACT

Objectives: To determine the safety of Sinopharm Covid -19 vaccine among health care workers of Khyber Teaching Hospital (KTH, Peshawar).

Material and Methods: This observational study was carried out to assess the side effects associated with the first dose of Sinopharm vaccine among health care workers in KTH Peshawar, Pakistan. Data was collected using a close ended questionnaire which was filled by the health care workers above 18 years of age. The participants were asked to monitor any side effects up to 1 week after the first dose of Sinopharm vaccine administered to them. Data was analyzed using SPSS version 23 for macbook.

Results: A total of 400 health workers were included in the study but only 155 participants responded by completing the questionnaire. It was observed that 63.9% of the participants who were vaccinated experienced at least one symptom after vaccination. The most common symptom was pain at injection site (36.8%) experienced during 15 – 30 minutes after vaccination followed by fatigue (21.3%), headache (18.7%), lightheadedness (12.3%), myalgia (10.3%). Percentage of other symptoms was less than 10%. The occurrence of symptoms after vaccination was greater in age group 24-42 years which was 60.6% while in age group 43-60 years it was 39.4%.

Conclusion: Our study concludes that Sinopharm vaccine has no or mild side effects and therefore safe for public use.

Key words: Safety, SARS Covid-19, Sinopharm vaccine

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INTRODUCTION

Coronaviruses belong to a group of viruses that cause respiratory diseases in humans. They are single stranded RNA viruses that get their name, "corona," from the many crown-like spikes on the surface of the virus [1]. Severe acute respiratory syndrome (SARS), Middle East respiratory syndrome (MERS) and the common cold are examples of coronaviruses that cause illness in humans [2].

Corona virus disease 2019 (COVID-19) is caused by SARS -CoV-2[3]. The new strain of corona virus, was first identified as outbreak of respiratory illness in Wuhan city of China[4]. It was reported to WHO on 31st December 2019 and declared as pandemic by WHO on 11th march 2020[5]. In Pakistan, on February 26th 2020, the city of Karachi reported the first case of coronavirus[6].

In the west, Italy had the highest number of COVID-19 mortalities while in the east, Iran had a high number of mortalities during the first wave[7]. There have been more than 2 million mortalities and 100 million plus people have been affected worldwide[8]. Rapid mutations in SARS-CoV-2 are responsible for the emergence of new variants of the virus in South Africa (1.351), United kingdom (B.1.1.7), Brazil (P.1) and India (B.1.617.2) and cause severe and rapid spread of Covid-19 infection mostly in unvaccinated individuals[9].

The mode of transmission of the virus is through respiratory droplets and each infected person can spread the infection to 2.2 other people[10].

Presentation of COVID-19 ranges from no or mild symptoms such as fever, cough and fatigue to severe pneumonia and multiorgan failure. Symptoms usually develop within 2 days to 2 weeks after exposure to the virus[11]

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Individuals above the age of 60 are at a greater risk of developing severe symptoms as compared to younger individuals who may be asymptomatic or have milder symptoms.[12]

Since the start of the pandemic many companies have been working on developing a vaccine. Despite being a long and expensive process, some vaccines have now made it to the market including Pfizer-BioNTech, Moderna, Oxford-AstraZeneca, Sputnik V, Novavax, Sinovac and Sinopharm.

Pfizer-BioNTech and Moderna are both mRNA vaccines. After the administration of the two doses in the American population, Vaccine Adverse Event Reporting System and v-safe reported 6,994 adverse effects out of 13,794,904 people who got vaccinated. However, 90.8% were mild adverse effects while 9.2% were severe including anaphylaxis.[13]

Oxford-AstraZeneca is a non-replicating viral vector vaccine. The efficacy of Oxford-AstraZeneca vaccine though clinical trials was 62.1% in individuals who got two doses.[14]

Sputnik is a Russian vaccine which also uses a non-replicating viral vector. The clinical trials show a protection of 92%.[15]

The company Sinopharm developed a whole virus vaccine in collaboration with the Wuhan Institute of Virology and the Institute of Biological Products. Phase III trials have been conducted in the United Arab Emirates, Bahrain, Peru, Serbia, Morocco, Argentina, Jordan and Pakistan[16]. On December 29th 2020, Sinopharm reported 79% efficacy[17]. The vaccine was licensed in China one day later and received emergency approval. The vaccine was allowed to be administered from the beginning of December 2020.

Even though the clinical trials show that Sinopharm vaccine offers protection against Covid-19, the duration of immunity is not known.

However, the specialized cells of our immune system, memory B cells, have the ability to hold information against antigens even for several years. According to Phase I/II trials the vaccine doesn't have the potential to cause severe side effects and stimulates the immune system to make antibodies against the virus[18].

METHODS AND MATERIALS

An observational study was carried out to assess the side effects associated with the first dose Sinopharm vaccine among health care workers in KTH Peshawar from 1st March 2021 to 31st March 2021 when according to the WHO policies, front health line workers and elderly people were first prioritized for Sinopharm vaccination in Pakistan.

Ethical approval was obtained from Institutional Review and Ethical Board (IREB), KMC reference number 671/DME/KMC dated 26/2/2021. The participants were asked to monitor any side effects up to 1 week after the first dose of vaccine administered to them. Data was collected using a close ended questionnaire which was filled by the participants fulfilling the inclusion criteria. Inclusion criteria included health care workers who received covid-19 vaccine and were above 18 years. Exclusion criteria included health care workers who were less than 18 years of age, pregnant and lactating mothers, patients who received monovalent antibodies/convalescent plasma, organ transplant in the past one year, immune deficient patients and those with history of anaphylaxis. Data was analyzed using SPSS version 23 for Macbook.

RESULTS

One Hundred fifty five health care workers, both males (73.5%) and females (26.5%),were included in our study, The occurrence of symptoms after vaccination was greater in age group 24-42 years which was 60.6% while in age group 43-60 years it was 39.4% as shown in table 1. Males had experienced more post vaccination symptoms (70.7%) as compared to females (29.3%) as shown in table 2.

It was observed that 63.9% of the participants who were vaccinated experienced at least one symptom after vaccination as shown in figure 2. Out of all the symptoms pain at injection site (36.8%) was the most common symptom reported followed by fatigue (21.3%), headache (18.7%), lightheadedness (12.3%), myalgia (10.3%), weakness (9.7%), dizziness (7.7%), nausea (7.1%), fever (6.5%), diarrhea (5.8%), tachycardia (5.2%) and redness at site of injection (5.2%). Percentage of other symptoms was less than 4% as shown in figure 1. Most people (43.9%) experienced at least one symptom within 15-30 minutes of getting the vaccine. Within 15-30 minutes the most common symptom experienced was pain at injection site. Only one male participant with known history of environmental allergy and a past history of mild/moderate reaction to a vaccine in our study reported wheeze within 3-7 days after getting the Sinopharm vaccine.

DISCUSSION

Several types of vaccines have been developed with different approaches making use of messenger RNA, spike proteins, non-replicating viral vector and inactivated whole virus. Each vaccine has different properties but they all act to activate the immune system. Sinopharm vaccine by China used the conventional approach of inactivated whole virus and claimed more than 70% effectiveness[19]. The virus was inactivated with B-propiolactone and injected intramuscularly to stimulate antibodies production against the infection[20]. The vaccine requires two doses with a span of twenty days from the first dose and may change to third dose in order to increase the effective re-

sponse of antibodies[21]. The clinical trials suggest that inactivated vaccine for SARS-CoV-2 is well tolerated with no serious side effects[22,23].

In our study we compared our findings of post vaccination symptoms experienced among health care workers with other published studies and clinical trials. It has been reported by Beijing Institute of Biological products/ Sinopharm that in phase II trials with 448 participants between age group 18- 59 years, 23% of individuals within first week of post vaccine experienced some side effects of which pain at the injection site was the commonest and only 2% people reported fever[24].

Another phase I/II trial by Wuhan Institute of products/Sinopharm revealed side effects that were mild and self-resolving. Among mild symptoms pain at injection site was the commonest side effect followed by fever[25]. Phase I randomized double-blinded controlled trials by Jing pu et al conducted among 191 participants at West China second University Hospital, Sichvan University, reported no serious side effect after vaccination with inactivated SarS- CoV-2 vaccine (Sinopharm). Mild symptoms commonly reported at injection site were redness, itching and swelling while common systemic side effects included fatigue[26].

An online of post vaccination analysis of multiple vaccines carried out in India by Rajeev Jayadevan et al observed that those who received Sinopharm vaccine, 24.4% experienced mild symptoms[27]. In our study, the results were almost similar to the above published studies and trials with pain at injection site being the commonest symptoms (36.8%), followed by fatigue (21.3%). There were no severe side effects reported.

Table 1: Percentage of symptoms after vaccination according to age

Age	Percentage (%)
24-42 years	60.6
43-60 years	39.4
Total	100

Table 2: Percentage of symptoms after vaccination according to gender

Gender	Percentage (%)
Male	70.7
Female	29.3
Total	100

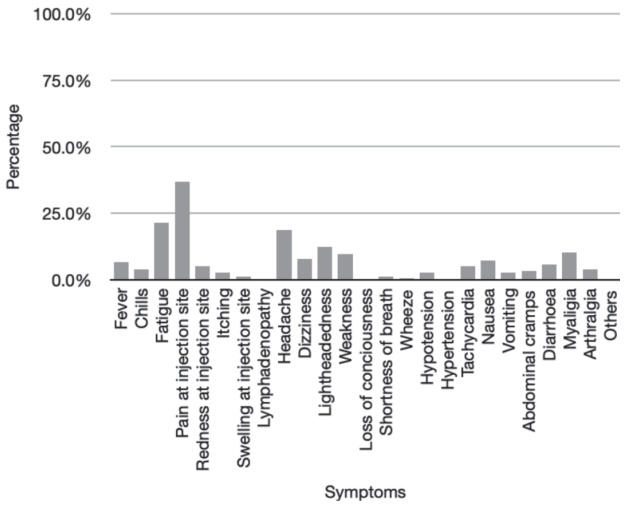

Fig 1: Percentage of symptoms experienced

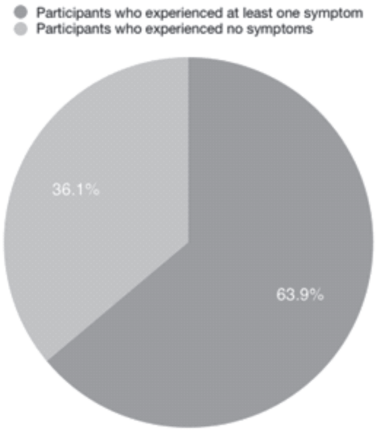

Fig 2: Percentage of participants who experienced at least one or no symptom

CONCLUSION

The findings of our study show no severe side effects among health care workers and is a contribution towards alleviation of public fear against vaccination which is a dire need to curb the spread of this newly infectious disease.

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AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under

Amer M: Idea, Concept, Statistical analysis

Altaf S: Bibliography, Literature review

Azhar A: Data collection

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

ORIGINAL ARTICLE

COMPARATIVE ANTIFUNGAL ACTIVITY OF WILD AND CULTIVATED LEAVES OF FICUS CARICA LINN

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ABSTRACT

Objective: The aim of this study was to compare the antifungal activity of wild and cultivated Ficuscarica Linn leaves extract.

Material and Methods: A cross-sectional analytic study was conducted in the Department of Botany Islamia College Peshawar from June 2016 to December 2016. After taking Permission from Botany department samples of two different species of wild and cultivated Ficus Carina plant were taken and analyzed for antifungal activity.

Results: Comparison of Zone of Inhibition in both Aspergillus niger and Aspergillus fumigatus colonies revealed that cultivated species of Ficuscarica Linn had more antifungal property against both the fungal species (63% and higher compared that to wild species having a maximum zone of inhibition of 54.54%), except for wild plant extract in the polar solvent such as chloroform which had a high level of antifungal activity (61.53%) only against Aspergillus fumigatus. The experiment also revealed that extracts from both wild and cultivated Ficuscarica Linn leaves in polar solvents such as methanol and chloroform showed a higher level of antifungal activity against both the fungal species compared to extract taken in non-polar solvents.

Conclusion: Extract from cultivated species of Ficuscarica Linn had a higher level of activity against both the fungal species i.e. Aspergillus niger and Aspergillus fumigatus, especially extract taken in polar solvents.

Key Words: Ficuscarica Linn, antifungal, tube dilution, zone of inhibition.

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INTRODUCTION

Pakistan's wide and diverse geological and climatic spectrum offers ecosystems to a very wide variety of plants. Many of these species have a pivotal role in medicine. According to a general survey of Pakistan about 6000 species of flowering plants exist in the country, out of which 600-700 are of medicinally important species[1]. Most local botanists believe this number of medicinally important plants to be an underestimation due to lack of research and effort. According to the drug bank statistics, there are a total of 14,315 drugs while the FDA reports the total number of prescription drugs to be over 20,000. About 85,000 valuable medicinal plant species are reported worldwide [2]. Given this information, one can infer that there is a lot more to plants to be used as medicines than human imagination. The history of plants to be utilized as medicines is rather ancient [3]. These plant materials initially took the form of crude drugs such as poultices, teas, powders, tinctures and many other herbal formulations. Not so long ago, it was discovered that the medicinal properties of plants are due to their active chemical compounds which produce a definite physiological action on the human body and the isolation of active compounds such as morphine from opium in the early 19th century made a revolutionary milestone in the history of medicine[4]. Since the earliest isolation of active ingredients from different plants, many essential drugs have been isolated such as aspirin from Salix alba, digoxin from Digitalis purpurea, quinine from Cinchona officinalis, atropine from Atropa belladonna and many other important drugs without which modern medicine would be obsolete. The most important of these bioactive constituents of plants are alkaloids, tannins, flavonoids and phenolic compounds. In the modern world use of plants in allopathic and homoeopathic medicine is an important component of the health care system in different countries of the world [5]. German herbal medicines constitute a fathomable example to help laymen understand the wide utility of plants as medicines. Thus, the utility of plants in pharmaceuticals for prevention, treatment and controlling different diseases needs no introduction but a brief discussion and mention reminds

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humankind of its utmost importance[6]. From being used as an additive to foods meant for pregnant women and nursing mothers for medicinal purposes to treat life-threatening infections due to antibiotic properties, the utility of plants in both traditional and modern medicine cannot be emphasized enough[7]. It has been observed through many studies that in developing countries there has been an increased shift towards the use of medicinal plants as therapeutic agents in comparison with pharmaceutical drugs. Although mass psychology and firm belief in the potential benefits of medicinal plants and their by-products might be a contributory factor in some developing communities which is mainly passed down through generations, alternative and complementary therapies based on plant remedies are getting popular by the day and even allopathic healthcare professionals in developed countries do not deny their role in treatment and prevention[8]. Safety and drug interaction regarding the usage of plants for medicinal purposes often raise a concern in people who go by the book and are not well versed in botany and biochemistry. Another group that shares and supports the congruent belief due to monopoly and monetary reasons are the pharmaceutical companies that make branded biochemical drugs. But the modern unbiased world is accepting the potential that plants offer in terms of therapeutic use[9]. Many of the plant-based medicines are now Food and Drug Administration (FDA) approved ensuring their quality and safety along with mentioning possible drug interactions. One important property of plants that have led to their use throughout history is their ability to kill bacteria, protozoa, viruses, fungi, animals and other unicellular and multicellular organisms. This property is often used and manipulated in a dexterous way by nature and by humans fit and beneficial to their needs. Many researchers have examined long-established uses of medicinal plants, but only a few studies have led to these ethnobotanical findings with laboratory jobs to confirm the real antimicrobial property of this plants[10]. Our study is an effort to contribute towards the authenticity of the activity in a specific plant species.

The rationale behind conducting this study is to find the antifungal activity of the fore mentioned plants. As pharmaceutical drugs have a lot of side effects, therefore, the need is to find benefits hidden in medicinal plants which are natural and have negligible side effects.

MATERIALS AND METHODS

This cross-sectional analytic study was conducted in the Department of Botany Islamia College Peshawar from June 2018 to December 2019. One sample of each variety of FICUS CARICA LINN wild and cultivated was taken and analyzed its chemical components were against antifungal properties. The agar tube dilution method was used as an antifungal assay to demonstrate the antifungal activity of the extract. The following fungal strains were used in this study:

Aspergillusniger.

Aspergillus fumigatus

Each strain was maintained on a Sabouraud dextrose agar (SDA) medium at room temperature.

The composition of Sabouraud dextrose agar medium was: Peptone complex 10mg/ml

Glucose 40mg/ml

Agar 15mg/ml

The samples for antifungal assay were prepared from an initial stock of 15mg of each plant extract sample per 10ml of Dimethyl Sulfoxide (DMSO). Slant cultures without extract were used for negative control. Data were analyzed using SPSS version 21.

LABORATORY PROCEDURE:

Media for fungus was prepared by dissolving 6.5 mg of Sabouraud dextrose agar in 100mldistilled water with the pH adjusted to 5.6. Test tubes were marked to 13cm mark. Sabouraud dextrose agar (commercial MERCK) was dispensed as 4ml volume into screw-capped tubes or cotton plugged test tubes and the test tubes were autoclaved at 1210 C for 20 minutes. The only single concentration of 15mg/10ml was made. Tubes were allowed to cool at 500 C and non-solidified Sabouraud dextrose agar was loaded with 100 μl of 15mg /ml plant extract which was inserted by compound pipette from the stock solution. Tubes were then allowed to solidify in a slant position at room temperature.

One slant of the extracted sample was prepared for each fungal species. The tubes containing solidified media and test compound were inoculated with a 4mm diameter piece of inoculum, taken from the seven-day-old culture of the fungi. Negative control test tubes without extract were also inoculated. The test tubes were incubated for 7 days at 280 C. Cultures were examined twice weekly during the incubation. Reading was taken by measuring the linear length of fungus in a slant position. Growth inhibition was calculated with reference to the negative control. Percentage inhibition of fungus growth for each concentration of compound was calculated by the following formula Percentage inhibition of fungal growth $=100 -$ Linear growth in test tube (mm) x 100 Liner growth in control (mm)

RESULTS

Antifungal activity of extracts from leaves of cultivated and wild species of Ficuscarica Linn against Aspergillus niger and Aspergillus fumigatus.

DISCUSSION

Our study was an attempt to demonstrate the medicinal value of Ficuscarica Linn and to demonstrate its antifungal activity. A local study conducted in 2013, which contrasts with our study revealed that neither bark nor

Table 1: Antifungal activity of extracts from leaves of cultivated and wild species of Ficuscarica Linn against Aspergillus niger and Aspergillus fumigatus.

Organism Organism	Plant Ficuscarica Linn	Leaves Extract	L.G.C(mm)	L.G.T(mm)	%Inhibition
Aspergillusniger	Cultivated Species	Methanol	110	70	63.63%
		Chloroform	110	60	54.54%
		n-hexane	110	45	40.90%
		Ethyl acetate	110	50	45.45%
Aspergillus fumigatus	Cultivated Species	Methanol	130	85	65.38%
		Chloroform	130	70	53.48%
		n-hexane	130	30	23.07%
		Ethyl acetate	130	25	19.23%
Aspergillus niger	Wild species	Methanol	110	60	54.54%
		Chloroform	110	45	40.90%
		n-hexane	110	30	27.27%
		Ethyl acetate	110	20	18.18%
Aspergillus fumigatus	Wild species	Methanol	130	70	53.84%
		Chloroform	130	80	61.53%
		n-hexane	130	40	30.76%
		Ethyl acetate	130	25	19.23%

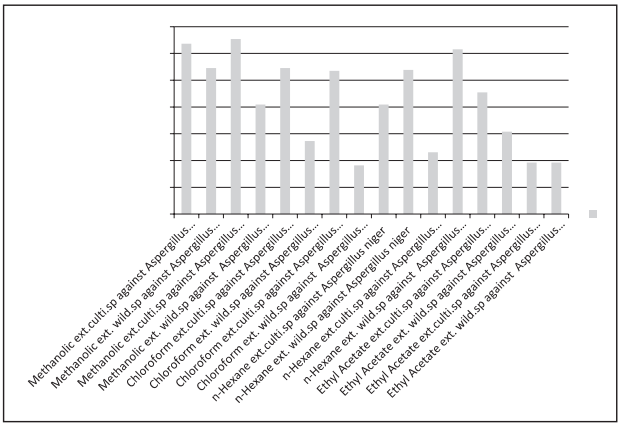

Fig 1: Comparison of Zone of Inhibition (%) of extracts from leaves of cultivated and wild species of Ficuscarica Linn against Aspergillus Niger and Aspergillus fumigates in methanolic (alternatively known as methanol), chloroform, n-hexane and ethyl acetate

leaves of Ficuscarica Linn had any antifungal potentials[11]. One of the possible explanations could be that they used a very potent antifungal drug (amphotericin B) as the standard/control in agar culture which was able to mask even the minute antifungal effect from fig extracts. Another possibility could be the chemical nature of one of the two solvents in which the extract from the plant was taken. The extracts of the four Ficus species had significant antibacterial activity in a study in Egypt but no antifungal activity was demonstrated in their study [12]. In contrast to this study, our study demonstrated antifungal activity. Although the four Ficus species did not include the Ficuscarica Linn species of the Ficus genus in the research, the antibacterial property was demonstrated in other studies. Similarly, a study in an Indian journal showed that Ficuscarica was rich in phytochemicals such as flavonoids, alkaloids and saponins[13]. Most of the antimicrobial activity was attributed to flavonoids. This study lacked any information regarding antifungal property due to a lack of sufficient evidence as fungal species were not used in the experiment. Likewise, a study in Morocco reinforced the antimicrobial, antitumor, antioxidant and antipyretic activity of Ficuscarica but the antifungal property was not included in the experiment [14]

A study conducted in Malaysia used the same types of solvents for sample preparations as was used in our study Ficuscarica had antifungal properties against seven fungal strains using disc diffusion method [15]. One noteworthy finding in their study was that Ficuscarica had wiped out one of the fungal population Candida albicans. A similar study conducted in Baghdad showed antifungal activity of Ficuscarica against three fungal strains and the same measure of the zone of inhibition was used as ours [16]. Another study conducted on Ficuscarica leaves revealed that the antifungal property of plants extracts from the Ficus genus was mainly due to the chitinases and chitinase like enzymes and antifungal activity was witnessed against Saccharomyces cerevisiae in the experiment[17]. There was an attempt to isolate two proteins from Ficuscarica in another study which proved that those two proteins had potent antifungal activity against six fungal strains used in the experiment and similar inhibitory zone measurements were taken as our study [18].

CONCLUSION

It is concluded that fig exhibits antifungal activity against a wide variety of fungal strains, signifying that fig

may indeed be used as a naturally occurring broad-spectrum antifungal drug. Moreover, what has come to the limelight in the study was that cultivated and domesticated fig has more to offer as an antifungal agent compared to wild fig.

LIMITATIONS

The shortcoming of the research was that we could not compare the findings with other studies showing the antifungal potential of Ficuscarica due to experimental differences. The differing nature of solvents, fungal strains, temperatures, exposure times, concentrations, units of measurements, parts of the Ficuscarica plant used limits us to compare the exact antifungal potency. We are, however, confident through findings in our study that antifungal property exists in Ficuscarica and the use of common fig as an antifungal agent can be compared to synthetic antifungal drugs, thus proving its health benefits scientifically and justifying the historical and ancestral use of this plant and its fruit for medicinal purposes.

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AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under

Ullah NB:	Data analysis, Manuscript Writing and Literature Review
Ali W:	Data collection
Iftikhar B:	Supervision and Review
Azhar S:	Manuscript Writing
Arif S:	Literature Review
ifitikhar S:	Data analysis and literature review
Jan S:	Data Collection

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

ORIGINAL ARTICLE

RISK FACTORS AND MANAGEMENT OF ANEMIA IN PREGNANCY

Saleha Sadeeqa, Samia Habib, Mubashara Saeed, Sania Shahid, Saba Ijaz, Anum Javaid, Sumera Latif

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ABSTRACT

Objective: This study was aimed to assess the dietary and socioeconomic factors associated with anemia in pregnancy and its management.

Materials and Method: A cross-sectional, descriptive study design was adapted using convenience sampling technique, involving 200 pregnant anemic women, during the period June-2018 to August- 2018 in different private and public sector hospitals of Punjab Pakistan. Data was collected through structured questionnaire and analyzed using SPSS version 20.

Results: Anemia was more prevalent (47.5%) among women aged 25-30 years. Significant association was found between gestational period and respondent' age (p=0.021) & educational level (p= 0.000). Hemoglobin level of patients was significantly associated with educational level (p = 0.000), location (p = 0.05) while tea/coffee consumption was significantly associated with educational level (p= 0.000) & location (p=0.022), protein diet consumption was significantly associated with age (p=0.001), educational level (p= 0.000) & location (p=0.000), vegetables & fruits consumption was significantly associated with educational level (p=0.003) and finally treatment option was significantly associated with age (p=0.015), education level (p=0.000) and location (p=0.000).

Conclusion: The study concluded that pregnant women of age group 25-30 years were at high risk of anemia. It is more prevalent in uneducated women and those living in rural areas. Healthy and fresh balanced diet rich in iron is recommended for health and good growth of the developing baby.

Keywords: Anemia, Pregnant, Hemoglobin, Mortality, Management

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INTRODUCTION

Anemia in pregnancy is common worldwide issue regarding public health and is characterized as hemoglobin levels less than 11 g/dl during the first and third trimester, and less than 10.5 g/dL during the second trimester[1,2]. It affects more than 56 million women globally[3]. According to WHO survey, more than half of the pregnant women are suffering from this disease[4] and is common among females aged 25-30 years[5]. Education reduces the risk of pregnancy anemia because of better knowledge on eating nutritious food [6,7]. Although it is common among developing countries, yet developed countries are not free from it; with high prevalence among rural areas than in urban areas[8].

Physiological adaptation during pregnancy causes hemoglobin dilution that leads to anemia[9]. Risks of iron deficiency anemia increases during second and third trimester,[10] that can lead to the premature birth, death of both baby and mother, perinatal mortality, growth restriction and low birth weight[11-13]. Pregnancy related anemia is observed to be common in third trimester[14]. In reference to previous studies lowest hemoglobin level observed during pregnancy was 3.5 gm/dl, highest was 12.9 gm/dl and average level were 9.5 gm/dl in a previous study [5].

Anemia is a multifactorial disease, such as Iron, folate, VitB12 deficiency, parasitic infections and malaria observed to be the primary causes of anemia[15,16] secondary to low education level, teenage pregnancy, poor socioeconomic status and short inter pregnancy interval[17]. Genetic factors and poor hygiene are other contributing factors[18].

Effective management of pregnancy anemia includes treatment of the underlying causes, restoration of the hemoglobin concentration, prevention and treatment of complications. This can be achieved with intake of healthy and balanced diet rich with iron and vitamins (meat, green vegetables, fruits etc) and prohibit intake of substances that reduce iron absorption (tea, coffee etc)[19]. Many studies have supported the strategy of supplementing pregnant women with iron and folic acid to increase the hemoglobin levels[20]. Treatment of pregnancy anemia includes intake of required supplements in accordance with diagnosis made. Most recommended supplements include oral elemental iron between 65-200 mg per day.

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When oral iron cannot be tolerated or is ineffective then IV iron replete iron stores[21,22]. Despite all, it is still a common cause of mortality and morbidity. This study is aimed to assess dietary and socioeconomic factors associated with pregnancy anemia and its management among pregnant females.

MATERIALS AND METHODS

A cross-sectional, descriptive study design was adapted using convenience sampling technique, during the period June-2018 to August- 2018. Data was collected from the department of Obstetrics and Gynecology of different private and public sector hospitals including Services hospital, Jinnah hospital, Lady Atchison hospital of Punjab-Pakistan. Data was collected through structured questionnaire and analyzed by using SPSS version 20.

Informed consent was obtained from all of the women who volunteered to participate. A structured questionnaire was designed to gather information which included questions related to patient's demography, diagnosis of anemia, risk factors, management and treatment of pregnancy anemia. Majority of the women completed their questionnaire themselves, while some were assisted. Data was analysed using SPSS version 20. Statistical significance was determined using chi square test $p \leq 0.05$ was considered as statistically significant. Study was approved from Institute of Pharmacy, Lahore College for Women University. Lahore. Permission to access patients was obtained from the gynecology and obstetrics department of the respective hospitals.

RESULTS

Results regarding patient demographics are presented in Table-1, which shows that 47.5% of the women were between the ages of 25-30 years, 33% females were having gestational age 21-25years, 11.5% females were found with gestational age >30yrs. Results for education level showed that 52% females were having primary education, 24% females were having secondary education, 16% females were having tertiary education, and only 8% of patients were not having any formal education. 32.5% female were from rural area and 67.5% females were from urban area. Association of gestational period with demographic characters is displayed in Table-2, which showed that 7.5% of females were in 1st trimester of pregnancy,16.5% females were in 2nd trimester, and 76.5% females were in 3rdtrimester of pregnancy. Significant association was found between gestational period and respondent' age ($p=0.021$) and educational level ($p= 0.000$). Association of hemoglobin level with demographic characters is displayed in Table-3, which showed that 75.5% females were having Hb level ranging b/w 7-10mg/dl, 22.5% of females were having Hb level >10mg/dl, and only 2% were having Hb level b/w 3-6mg/dl. Significant association was found between Hb level of patients and education level ($p = 0.000$), location ($p = 0.05$).

Association of dietary habits with demographic characters is displayed in Table- 4, which showed that 81% females were taking tea/coffee and significant association was found between tea/coffee consumption and education level ($p= 0.000$) and location ($p=0.022$). A total of 18% females were taking protein diet and significant association was found between protein diet consumption and age ($p= 0.001$) education level ($p=0.000$) and location ($p=0.000$). A total of 74% females were taking vegetables and fruits and significant association was found between vegetables and fruits consumption and education level ($p= 0.003$). Association of treatment options with demographic characters is displayed in Table-5, which showed that 41.5% patients were recommended for treatment with iron supplements & improved diet both, 6.5% were taking oral supplements, 27% were administered with iron IV, 23% were advised to improve diet, and only 22% patients were recommended for blood transfusion. Significant association was found between treatment options and age ($p=0.015$), education level ($p=0.000$) and location ($p=0.000$).

DISCUSSION

Pregnancy anemia being common and prevalent problem was observed to be common among the females having age ranging between 26-30years. Results seem to be in accordance with the results of previous studies5. The results regarding effect of education on prevalence of pregnancy anemia showed that it was more prevalent in less educated or uneducated women, previous studies supported this outcome that this condition is prevalent among uneducated females [5,6].

Results further showed that 76.5% females were in 3rd trimester, 16.5% in 2nd trimester, and 7.5% in 1st

Table 1: Patient's demographics

Variable	Frequency (N=200)	Percentage %
Gestational age of patient		
16-20yrs	16	8
21-25yrs	66	33
26-30yrs	95	47.5
>30 yrs	23	11.5
Level of education		
No formal education	16	8
Primary	104	52
Secondary	48	24
Tertiary	32	16
Area		
Urban	135	67.5
Rural	65	32.5

Table 2: Association of gestational period with demographic characters

Variable	Frequency (%)	Demographic Character	P –Value
1st trimester	15(7.5)	Age	0.021
2nd trimester	33(16.5)	Education level	0.000
3rd trimester	152(76.5)	Area	0.706

Table 3: Association of hemoglobin level with demographic characters

Variable	Frequency (%)	Demographic Character	P –Value
3-6 mg/dL	4(2)	Age	0 .640
7-10 mg/dL	151(75.5)	Education level	0 .000
>10 mg/Dl	45(22.5)	Area	0.05

Table 4: Association of dietary habits with demographic characters

Variable	Frequency (%)	Demographic Character	P –Value
Tea consumption			
Yes	162(81)	Age	0.164
No	38(19)	Education level	0.000
		Location	0.022
Protein diet consumption:			
Yes	36(18)	Age	0=.001
No	164(82)	Education level	0=.000
		Location	0.000
Vegetables and fruits consumption:			
Yes	148(74)	Age	0.996
No	52(26)	Education level	0.003
		Location	0.127

Table 5: Association of treatment options with demographic characters

Treatment options	Frequency (%)	Demographic Character	P-Value
Iron supplements	13(6.5)	Age Education level Location	0.015 0.000 0.000
Iron IV	54(27)		
Improving diet	46(23)		
Iron supplements & Iron IV	43(21.5)		
Blood transfusion	44(22)		

trimester. This result is supported by previous studies that showed increased chances of pregnancy anemia during 2nd and 3rdtrimester[14]. Results regarding hemoglobin level showed that 2% females were having Hb level within 3-6mg/dl, 75.5% were having within 7-10mg/dl, and 22.5% were having greater than 10mg/dl. This outcome is supported by the previous research[5].

Assessment of dietary intake of patient showed that anemic condition is prevalent among coffee/tea takers and is prevented by eating balanced diet, consisted of proteins, vegetables and fruits findings are supported by other studies19. 27% of patients were recommended for iron administration through IV route, 23% patients were advised to improve diet, 21.5% patients were advised to take iron supplements with improvement of their diet, 22% were recommended for blood transfusion. These findings are consistent with recommended treatment methods[20,21,22].

CONCLUSION

Anemia is global health condition affecting more than half of the pregnant females. According to the present findings it is concluded that females during 2nd and 3rd trimester are at verge of developing anemia. Iron deficiency is considered as the primary reason. This condition is prevalent among the females of reproductive age were majority of them were uneducated. Intake of healthy balanced diet, with iron supplements before and during pregnancy tends to control the severity of condition.

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AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under

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Shahid S:	Acquisition and critical review
Habib S:	Analysis and interpretation of data
Saeed M:	Final approval
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Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

ORIGINAL ARTICLE

MICROBIOLOGICAL QUALITY ASSESSMENT OF RAW COWS MILK IN PESHAWAR DISTRICT

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ABSTRACT

Objective: To study the microbial analysis of raw cow's milk collected from selling points of Peshawar.

Materials and methods: A total of 80 aseptically raw milk samples were collected by multistage sampling technique from four towns of Peshawar in sterile glass bottles and stored in ice containers for laboratory analysis at Agriculture University Peshawar. Microbial analysis was performed on plate count and samples were screened for staph aureus, E.coli spp, and salmonella spp. The microbiological load was tested and the data were analyzed by Statistical Package for Social Sciences (SPSS) version 20.

Results: The microbial analysis of milk revealed contamination of milk and the most prevalent bacteria was Escherichia coli (26.2%) and the least prevalent was Salmonella spp (3.75%).

Conclusion: Although the presence of E.coli spp, staph spp, and Salmonella spp. indicate that the milk is contaminated but found that the total bacterial count was within the permissible limit. If not controlled in time will lead to public health issues. This highlights an urgent need to adopt good sanitary practices and monitoring of milk from production to distribution by the health authorities.

Key Words: Microbial analysis, raw cow's milk, E.coli spp, staph spp

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INTRODUCTION

The farm animals industry in a country like Pakistan is facing a lot of challenges like poorly developed animal husbandry and diseases that are affecting the quality of milk being produced. Bacterial contamination of milk is a common problem faced by the dairy industry, especially in developing countries. When the animal is diseased, bacteria can gain access to the milk from the primary source, as in the case of mastitic milk. Secondary bacterial contamination in milk is prevalent, and it is linked to an unsanitary milk supply chain[1,2]. When milk becomes contaminated with bacteria, it spoils quickly and also, could be a source of milk-borne illnesses in humans. Studies reveal that pathogenic bacteria such as Brucella abortus, Escherichia coli 0157: H7, Mycobacterium Bovis, Campylobacter jejuni, Salmonella spp., Clostridium spp., and Staphylococcus aureus cause up to 90% of all dairy-related disorders[3,4,5].

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Escherichia coli organisms are the most common contaminants of raw and processed milk.[6] In a study, 65% of raw milk tested in Malaysian dairy farms were positive for Escherichia coli[7] whereas 74% of the samples were contaminated with E Coli in a study in Turkey. [8] Staphylococcus Aureus due to its ability to produce enterotoxin, is an important cause of milk-borne diseases in humans. Staphylococcus Aureus strains has been isolated from hands of milking persons and dairy cows. A study in Iran in 2015 on 1930 samples of raw cow milk, showed the prevalence of Staphylococcus Aureus as 12.4% [9]. Salmonella contamination can either be due to infected persons or contamination of environment or by consumption of raw milk or its products[10]. Studies in Rawalpindi and Islamabad revealed that infection with Salmonella were as low as 6% as compared to other microbes [11].

Peshawar is one of the major city of Pakistan, having a population of 2,203,000 [12]. Milk for consumption, comes not just from the city's surrounds, but also from the interiors of other districts. Despite having a substantial amount of milk supply, manufacturing, delivery, and storage conditions are all still done in traditional ways. In such circumstances, the possibility of milk-borne illness is a major public concern[13]. Milk, on the other hand, travels through numerous hands from producer to consumer, and as a result, the quality of milk reaching customers is frequently substandard, both from a hygienic and nutritional

standpoint. There is a scarcity of information on microbial pathogens in milk in Peshawar, therefore, this study was an attempt to perform the microbial analysis of raw cow's milk collected from selling points of Peshawar.

MATERIALS AND METHODS

A cross-sectional descriptive study was conducted in Peshawar district and laboratory work was done at Agriculture University Peshawar. Multistage sampling technique was adopted where Peshawar was divided into four towns, TW-1 (Town 1, L-1 Sikandar Town, L-2 Gul Bahar), TW-2 (Town 2, L-3 Shahi Bala, L-3 Pajjagi), TW-3 (Town 3, L-5 University Road, L-6 Hayatabad), TW-4 (Town 4, L-7 Hazar Khawani, L-8 Badaber) samples were collected.

Sample size was calculated according to WHO sample size formula as $n=z^2pq/d^2$. A total quantity of 80 samples of raw milk were collected at selling points aseptically in sterile glass bottles. The collected samples were shifted to the University of Agriculture Peshawar, Department of Animal health for analysis laboratory for processing on ice packs maintaining 6-8 °C. A total of 20 milk samples were collected twice a week for four weeks. Microbial Analysis of Milk: The total plate count evaluation standard pour plate technique was followed. Tenfold dilution was standardized 1 ml of milk sample to 9 ml of Normal saline solution (NSS). Dilutions were standardized and quantity of 0.1 ml inoculums from 10^{-3} and 10^{-4} dilutions were processed on pour plate technique and agar was poured and mixed thoroughly by rotating the plates. The plates were incubated for 24 hours at temperature of 37˚c. Total plate counts were calculated by using standard formula[17].The bacterial colonies were counted with the help of the bacteriological colony counter (MAC) and colony forming (CFU) was counted by using the formula below.

$$\text{Log}_{10}\text{CFU/gm} = \frac{\sum C}{[n1+(0.1\times n2)]\times d}$$

Where, $\sum C$ = Total number of colonies counted from all plates, n1 = No. of plates of lower dilution, n2= No. of plates of higher dilution, d= Dilution factor

Staphylococcus Aureus Count: 1ml of raw milk were placed for Staphylococcus Aureus, isolation in each decimal dilution and were patterned on the surface of pre solidified (mannitol salt) medium for 37°C for 48 hours and colonies were counted on colony counter under microscope expressed and calculated.Salmonella Count: About 25ml of raw milk were added to 225 ml of sterilized buffered peptone water and incubated at 37°C overnight and colonies were counted. Escherichia Coli Count: Dilutions were made by withdrawing 1ml of raw milk sample into 9ml of 0.1% sterilized buffered peptone water and then further serial dilutions. A 10 μL was drawn from appropriate dilutions and placed on MacConkey Agar. Spread the sample on agar by sterile glass rod, and plates were incubated at 37°C for 24 hours. The colonies were counted. The data were analyzed by Statistical Package for Social Sciences (SPSS) version 20.

RESULTS

Three bacteria namely Staphylococcus Aureus13 (16.2%), E.coli 21 (26.2%) and Salmonella spp 03 (3.75%) were isolated and identified in the present study area. Out of 80 samples 37 (46.2%) were contaminated with different bacteria's like 26.2% was E Coli , 16.2% was staphylococcus and 3.75% was salmonella species see table 1 for details. See table 2

Table 1: Frequency of bacteria isolated from milk samples collected from different selling points of Peshawar

Bacteria Isolated	Bacteria isolated from milk samples								Total (%)
	TW1		TW2		TW3		TW4		
	L-1	L-2	L-3	L-4	L-5	L-6	L-7	L-8	
Staphylococcus	02	01	03	02	0	01	02	02	13 (16.2%)
E.coli	03	01	04	01	02	03	05	02	21 (26.2%)
Salmonella spp	00	00	01	0	01	00	01	00	03 (3.75%)
Total	05	02	08	03	03	04	08	04	37 (46.2%)

TW-1 (Town 1, L-1 Sikandar Town, L-2 Gul Bahar), TW-2 (Town 2, L-3 Shahi Bala, L-3 Pajjagi),
TW-3 (Town 3, L-5 University Road, L-6 Hayatabad), TW-4 (Town 4, L-7 Hazar Khawani, L-8 Badaber)

Table 2: Frequency of bacteria isolated from milk samples collected from different selling points of Peshawar

Milk selling point	Positive samples	Average bacterial count of samples							
		Total Plate Count		Total staph Count		Total E. Coli Count		Total Salmonella Count	
		CFU/ml	Log	CFU/ml	Log	CFU/ml	Log	CFU/ml	Log
TW-1	07	660,378	5.81	508.12	2.70	243.72	2.38	115.04	2.06
TW-2	11	540,230	5.73	430.23	2.63	205.14	2.31	125.01	2.09
TW-3	07	620,538	5.79	460.09	2.66	228.10	2.35	109.21	2.03
TW-4	12	756,400	5.87	538.07	2.73	271.23	2.43	121.06	2.08

TW-1 (Town 1, L-1 Sikandar Town, L-2 Gul Bahar), TW-2 (Town 2, L-3 Shahi Bala, L-3 Pajjagi),
TW-3 (Town 3, L-5 University Road, L-6 Hayatabad), TW-4 (Town 4, L-7 Hazar Khawani, L-8 Badaber)

DISCUSSION

In our study the difference in value of the total viable count might be due to unhygienic practices of milking. The unhygienic condition of the milking methods may cause a high burden of pathogenic bacteria in milk. The bacterial count may be due to environmental condition of barn and malpractice cleanness at the time of milking, storing and transportation enhanced bacterial growth especially salmonella spp from contaminated objects during handling [14, 15].

The improper hygienic condition leads to contamination of milk with high plate count value as reported by different studies in Badin, Pakistan, and studies in Ethopia[16,17,18]. While in my study only salmonella species count was high.

It was reported that high plate count can be subjective of poor storage, faulty milking, hygienic condition of cow barn and milking and storage kits[19,20,21,22] which were consistent to our findings.

The contamination of each isolated bacteria were higher across the selling points. The level of contamination a study done at Ethopia revealed Staph aureus were higher in collecting points [23] while our study also had similar contamination.

Another study done at Ethopia also supported our study findings that milk contamination involved unhygienic practices pre milking as udder cleanliness, unhygienic status of milk handlers and post milking involved sanitation of storage tools and contamination during transportation on roadside [24].

It has been reported in a study in Nigeria that high isolation frequency of Staph aureus (38 %), E.coli (24%) and Salmonella spp (2%) from milk at various retails points [25]. While our study had low staph aureus and high E Coli and salmoneela spp.

However, it has also been reported that even in hygienic circumstance milk comprises microorganism which may either resulting from milk ducts or additional contamination either may come from milking equipment and milk handlers[26]. Similar, studies conducted in Ethiopia to assess contamination of milk, with a higher frequency of E.coli was observed across market chain [17].

The isolation of staph aureus, E. coli and salmomella spp pointed out that milk samples indicated risk of enteropathogenic bacteria [25,27] and same is true in our study. Limitations of my study were no access to dairy farms and financial constrains as the tests were costly.

CONCLUSION

Although the presence of E.coli spp, staph spp and salmonella spp. indicate that the milk is contaminated due to external sources possibly due to fecal pollution from cows dunk and having public health significance but it was found to be within permissible limit, except for salmonella spp and if not controlled will lead to public health issues. It is recommended that the community awareness might be imitated among the farmers for hygienic milk production and processing. Hygienic practices like hand washing by the milk handlers and pasteurization by the consumers etc are recommended to be applied.

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AUTHOR'S CONTRIBUTION

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Alam A:	Concept, data collection, article writing
Akhtar A:	Data collection, article writing
Gul R:	Data collection, article writing, Data Analysis
Rehman R:	Data collection, Referencing

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

THE PREVALENCE OF CHRONIC HEPATITIS C IN PATIENTS PRESENTING WITH VAGUE RHEUMATIC SYMPTOMS IN A LOCAL COMMUNITY IN DISTRICT PUNJAB, PAKISTAN

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ABSTRACT

Objective: This study was aimed to determine the prevalence of chronic hepatitis C in patients presenting with vague rheumatic symptoms in a local community in district Punjab, Pakistan.

Materials and methods: A cross-sectional study was conducted in Tehsil Headquarter Hospital Sharaqpur Sharif, Sheikhupura, Pakistan. During a period of two and a half months, 751 patients presenting to general outdoor department with vague symptoms were selected through random sampling. People who presented with symptoms related to rheumatic dieases including, arthralgia, myalgia and lassitude without being explained on any other organic diseases, were labelled as vague symptoms. They were tested for Anti Hepatitis C Virus Antibodies, Hepatitis B Surface Antigen, and Anti Human Immunodeficiency Virus Antibodies with Rapid Immunochromatographic Test Kits. Statistical analysis was performed using IBM SPSS Statistics version 23.

Results: Of the 751 randomly selected patients, 28 were eliminated from results due to missing data and another 156 were removed on the basis of exclusion criteria. Out of 564 included participants, 37.8% were male and 62.2% were female with a mean age of 53.11±11.2 years. Twenty-seven percent of people screened with vague symptoms were found to be positive for Hepatitis C (N=152), 2.3% were Hepatitis B (N=13), whereas only one was HIV positive.

Conclusion: This study suggests that Chronic Hepatitis C often present with vague rheumatic symptoms like arthralgia, myalgia and lassitude. Patients presenting with such symptoms and without underlying rheumatic diseases should be screened for hepatitis C virus infection.

Keywords: Chronic Hepatitis C, vague symptoms.

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INTRODUCTION

Hepatitis C infection is a global threat to health. Its prevalence is believed to be 2·5% of the total world population (177·5 million), with the highest being in Central Asia and Central Africa (>3·5%), moderate in the East, South and Southeast Asia, West and East Africa, North Africa and Middle East, Southern and Tropical Latin America, Caribbean, Australasia, and Eastern Europe (1·5%-3·5%) and relatively low (<1·5%) in Southern Africa, North America, Andean and Central Latin America, Pacific Asia and Western and Central Europe[1]. However, in Pakistan there is great variability of prevalence with limited data available. According to the data currently available that includes both published and unpublished papers, prevalence in Pakistan among the general population is 6·8%[2].

HCV has been a culprit of millions of deaths globally every year (1·3 million)[3]. Chronic hepatitis C has served as a major distress for families by significantly reducing the quality of life[4]. However, not all patients suffer severe complications.5 In fact, the initial stage HCV infection is usually asymptomatic or mild. According to published studies, fatigue is the most common symptom of HCV infection followed by rheumatic symptoms like myalgia, arthralgia, lassitude, and depression[6,-12] . The initial mild nature results in a number of people to stay undiagnosed and remain chronic carriers. They are diagnosed when they develop signs and symptoms of liver failure [13].

Despite being aware of these facts, educating people about the disease and performing screening tests still remains a challenge in Pakistan [14]. With overburdened hospitals and deficient investigative facilities, a large number of people are neglected. There are limited resources and lack of health facilities in the peripheral areas and that corresponds to the very high prevalence rates in rural areas [15]. Illiteracy and poor economic status add to this

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misery and people do not focus on their health until they become very sick.

This study was focused on highlighting the prevalence of HCV infection in patients presenting with vague rheumatic symptoms such as lassitude, myalgia and arthralgia in the periphery of district Sheikhupura, Punjab, Pakistan.

MATERIALS AND METHODS

This cross-sectional study was conducted in Tehsil Headquarter Hospital Sharaqpur Sharif, a Secondary Level Hospital under Primary and Secondary Health Care Department, Government of Punjab. It is located in Tehsil Sharaqpur Sharif, a small town in District Sheikhupura of Punjab, Pakistan having a population of about 40,000 people. Minimum sample size calculated using OpenEpi Version 3 was 287 at 95% confidence level. However, 751 participants were randomly selected from routine outdoor patients, who presented with vague rheumatic symptoms. For the purposes of the study "Vague symptoms" included myalgia, arthralgia, malaise and lassitude. Inclusion criteria for the study included, age above 40 years for both genders and rheumatic symptoms without organic explanation for those. Exclusion criteria included, overt jaundice and anemias, uncontrolled Diabetes Mellitus, Hypertension, Rheumatological disorders, and Hypothyroidism were ruled out on the basis of medical history and general physical examination. Those who met the inclusion criteria were briefed regarding the procedure of the study and informed consent was obtained. They were then screened for Hepatitis C Virus, Hepatitis B Virus and Human Immunodeficiency Virus with Rapid Immunochromatographic Test Kits, following manufacturer's instructions. Kits were manufactured by Vaxper Inc. Miami, Fl, USA. For statistical analysis, SPSS version 23 was used.

RESULTS

Among a total 751 subjects, 28 were eliminated from results due to missing data and another 156 were removed due to exclusion criteria. Out of 564 included participants, 37.8% were males (N=213). Remaining 62.2% were females (N=351). The mean age of subjects is shown in Table 1. Hepatitis C Virus was detected in 26·95% subjects (N=152) out of which, 41·44% are males (N=63) and 58.55% are females (N=89). Gender-wise prevalence of Hepatitis C is shown in Figure 1. HBsAg was detected only in 2.3% people (N=13) out of which, 8 were female and 5 were male. Only one patient was positive for HIV antibodies. Comparison of prevalence of Hepatitis C and other viral infections is shown in Figure 2.

DISCUSSION

This study highlights a high prevalence of hepatitis C in the peripheral areas of Pakistan. Although international literature suggests a global decline in HCV prevalence in the past few years, this high prevalence and review of available material suggests that the incidence of HCV is still rising in Pakistan. This emphasizes the need for updating statistics. From 2010 to 2015, there are only 86 studies on prevalence of HCV that includes published papers in indexed, non-indexed journals, and unpublished studies

Table 1: Mean Ages of the study participants

	Mean	N	Standard deviation
Male	55.40	213	21·12
Female	52.12	351	87·10
Total	36·53	564	49·11

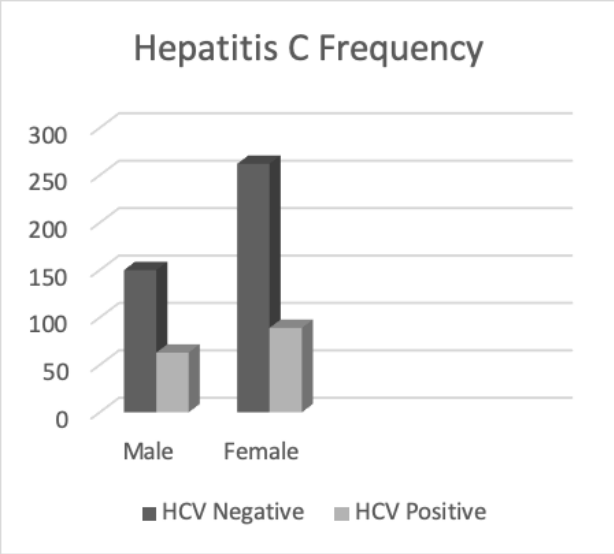

Fig 1: The frequency of HCV in males and females

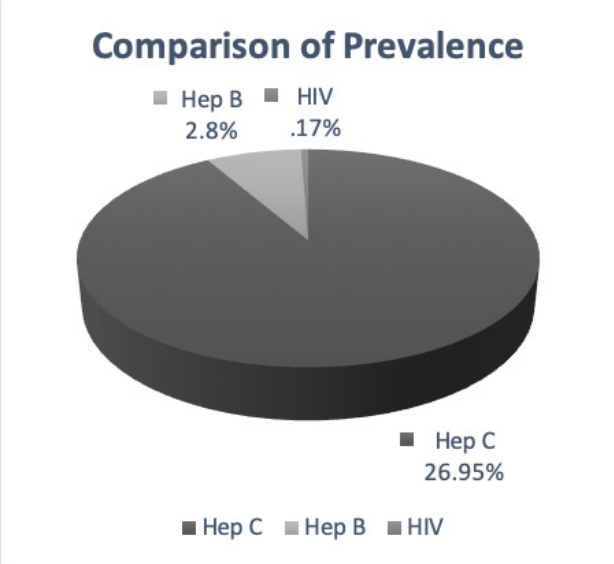

Fig 2: Comparison of prevalence of HBV and HCV in study population

as well [2]. It is noteworthy that there is high parity in this data. The overall prevalence in general population according to this data is 6·8% whereas it is reported to be 3·8% by the global prevalence studies published in indexed journals [16].

Among the general population, Hepatitis C is presumed to be a serious disease but most people remain unaware of the symptoms and phases of the disease which is a major factor in delayed diagnosis and increased morbidity and mortality of hepatitis. Also, in overburdened healthcare setups, due to a deficiency of resources and the clinical impression of hepatitis C being a moderate to severe disease notably in young doctors, many a times these patients get neglected. From this study, it is evident that a considerable proportion of people who presented with vague and mild rheumatic symptoms in the general out-patient departments were found to be positive for HCV. So, a more vigilant approach towards such patients is necessitated. Emphasis should be paid towards augmentation of clinical picture, symptoms and clustering of symptoms to improve diagnosis and overall management of Chronic Hepatitis C [17].

The presence of vague and mild symptoms indicates a recent infection and curable stage of the disease. So, there is a dire need of expansion of hepatitis control program throughout the country, especially in peripheries, where people are relatively uninformed regarding this disease. This should include both screening and education to diagnose patients in time and stop the spread [18].

Also, amidst the ongoing hepatitis control program throughout the province, this high prevalence is alarming. This calls for a need to check the efficacy of these control programs and reassess the strategies accordingly [19]. High prevalence of infection in people with a history of medical and surgical interventions along with blood transfusions is evident. That may be attributed to malpractice. There is a significant role of quacks who are involved in needle usage and unsafe use of intravenous drugs and surgical instruments [20]. Moreover, many hospitals also lack sufficient safety protocols and practice, including improper sterilization, lack of standard medical hygiene, careless handling, lack of proper disinfection, improper waste disposal, and untrained staff, which have been reported several times specifically in rural areas [21]. Strict and immediate action is required to develop updated SOP's and ensure strict compliance to stop the spread of hepatitis C virus. A complete revamping of patient education system is necessary according to cultural requirements. Currently the main source of patient education for infectious diseases is print media to which a large population is unresponsive. Therefore, awareness should be given to people regarding the transmission, signs and symptoms, precautions, treatment, and complications in effective ways.

Various limitations of this study should be noted. Firstly, we could not report prevalence of individual symptoms. Secondly, due to limitations in diagnostic facilities, we could not rule out certain other causes of fatigue and generalized body aches; such as Vitamin D3 levels and other chronic diseases [22].

CONCLUSION

This study suggests that Chronic Hepatitis C often present with vague rheumatic symptoms like arthralgia, myalgia and lassitude. Patients presenting with such symptoms and without underlying rheumatic diseases should be screened for hepatitis C virus infection.

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The completion of this study could not have been possible without the assistance of many people including Dr. Danish Islam and the Paramedical Staff at Tehsil Headquarter Hospital Sharaqpur Sharif. We would like to particularly thank Dr. Fatima Zaidi and Dr. Qanita Mahmud (Assistant Professor of Physiology, University College of Medicine) for reviewing and supervising the study.

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Following authors have made substantial contributions to the manuscript as under

Sarwar F: Concept, Design and Proof reading

Murtaza G: Acquisition and critical review

Javad S: Analysis and interpretation of data

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

REVIEW ARTICLE

SYSTEMIC AND LOCAL DELIVERY OF ANTIBIOTICS IN MANAGING PERIODONTAL DISEASES: AN UPDATE

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ABSTRACT

Objective: The aim of this update was to evaluate the use of local and systemic antibiotics for the treatment of periodontal diseases. PubMed and google scholar databases were used to search through the past 30 years of literature using selected search criteria "Periodontal diseases*[TW] AND (gingivitis*[TW] OR periodontitis*[TW] OR antibiotics*[TW])" to identify articles/book chapters discussing polymerization shrinkage and possible solutions. In total, 46 articles/book chapters met the criteria for inclusion in the literature review.

Due to the accumulation of bacteria in the form of dental plaque, the tissues and bone surrounding the teeth can become infected leading to periodontal diseases such as gingivitis and periodontitis. The main purpose of periodontal therapy is to eliminate or control the undesired effects of these bacteria present in the oral cavity in the form of biofilms. The use of antibiotics in conjunction with mechanical instrumentation has been suggested for the successful treatment of periodontal diseases.

It can be concluded that the use of antibiotics is justified in cases with rapid signs and symptoms of destruction of periodontal tissues. Hence, antibiotics are suggested in cases of aggressive periodontitis, periodontal abscess, necrotizing ulcerative gingivitis, necrotizing ulcerative periodontitis and periodontitis that do not respond well to mechanical instrumentation alone. However, antibiotics may cause side effects and the bacteria may develop resistance, therefore dentists should keep in mind the adverse effects and benefits while prescribing antibiotics. Moreover, antibiotics should always be given as an adjunct to mechanical instrumentation and oral hygiene instructions to achieve successful outcome.

Keywords: Periodontal diseases, gingivitis, periodontitis, local antibiotics, systemic antibiotics.

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INTRODUCTION

In ideal conditions, every individual wants natural healthy teeth throughout their life for aesthetics, form and function. However, due to accumulation of bacteria in the form of dental plaque, the tissues and bone surrounding the teeth can become infected which can be termed as periodontal disease[1]. (Table 1) Periodontal diseases are inflammatory disorders of chronic nature and can include gingivitis and periodontitis. Gingivitis is defined as inflammation of gingiva only, while periodontitis is inflammation of tissues around teeth which can result in loss of surrounding ligaments and alveolar bone, eventually leading to loss of teeth from the sockets.[2,3] The main difficulty in managing periodontal diseases arises from the bacteria which are not only present in the biofilm but also present throughout the oral cavity, thus making them almost impossible to eliminate.[4] To prevent the loss of teeth, periodontal therapy is performed which aims to eliminate or reduce the amount of pathogens by mechanical debridement.[5] However, due to surface anomalies on the teeth and adjacent epithelium, certain bacteria may still remain in periodontal pockets resulting in recolonization and making the mechanical debridement less effective.[6] Moreover, certain individuals do not respond well to mechanical therapy, therefore, many dentists and microbiologists appreciate the use of antibiotics.[6,7] Antibiotics help in reducing the amount of bacteria, thus helps in decreasing the inflammation of diseased tissues.[8] Haffajee reported a

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clinical study in which he found increased clinical attachment gains and decrease in number of pathogens when treated with antibiotics as an adjunct to root surface instrumentation (RSI).[9] Main reason for the use of antibiotics could have been the realization during 1970s that certain types of bacteria were involved in periodontal diseases.[10] Since then, the use of antibiotics became an interesting element of periodontal therapy.

MATERIALS AND METHODS

Electronic search of PubMed/Medline and google scholar databases was done. A total of 647 articles were evaluated and screen for parameters including periodontal diseases and the use of antibiotics in relation to periodontal diseases. The search was carried out using the following criteria "Periodontal disease*[TW] AND (Gingivitis*[TW] OR Periodontitis *[TW] OR antibiotics*[TW])". The studies that were duplicate, not in English language and not published in dental journals were excluded. Studies published between the years 1990 and 2018 that evaluated the periodontal diseases, there management and treatment strategies or reported strategies for treating periodontal diseases and use of antibiotics for inclusion. In the end, 46 articles/book chapters were included in the study for review (Fig.1)

ROLE OF ANTIBIOTICS

It is reported that antibiotic resistance of bacteria present in biofilm is 1000-1500 times greater than the bacteria present as pure cultures.[11] Moreover, use of antibiotics alone for the treatment of periodontal disease can be insufficient, therefore, for successful results, antibiotics should be given in combination with RSI.[9,12] According to the 6th consensus statement on periodontology, it can be suggested that systemic antibiotics should be administered on the visit in which mechanical debridement is completed.[13,14] On the other hand, locally delivered antibiotics should be placed soon after RSI.[10] There are several mechanisms by which the antibiotics affect the pathogens like inhibiting the cell wall synthesis, inhibiting ribosomal protein synthesis, suppressing DNA synthesis, inhibiting folic acid synthesis and altering the cell membrane permeability.[15] Ideally, antibiotic sensitivity and culture testing of plaque samples should be carried out before selection of antibiotics.[10,16] There are a variety of antibiotics which are used in management of periodontal diseases and they can be either systemically administered or locally delivered.

SYSTEMIC VERSUS LOCAL ADMINISTRATION OF ANTIBIOTICS

Most common route for systemic antibiotics is oral administration. However, in some cases intravenous or intramuscular injections of antibiotics can be given. On the other hand, locally delivered antibiotics can be placed in periodontal pockets by various drug delivery systems. These systems may include fibers, films, strips and polymers (biodegradable and non-biodegradable).[17] According to Mombelli,[18] systemic antibiotics are distributed throughout the body resulting in lower concentration in periodontal pockets but might be effective against bacteria that are present elsewhere in the oral cavity such as tongue and tonsils. Moreover, administration of systemic antibiotics can cause some side effects, resulting in poor patient compliance.[18] On the other side, locally placed antibiotics achieve higher concentration but are only effective against bacteria confined to that specific site. Moreover, locally placed antibiotics require minimum patient compliance and have negligible adverse effects.[18]

COMMONLY USED ANTIBIOTICS

Tetracycline: Tetracycline acts against gram positive as well as gram negative bacteria.[7,19] Derivatives of tetracycline are also present which are doxycycline and minocycline and these derivates are more lipophilic, thus they can be administered in low doses.[7] Tetracycline is a bacteriostatic antibiotic when administered systematically and acts by inhibiting protein synthesis in bacterial cell.[19] However, upon local administration of tetracycline in pockets, it acts as bactericidal.[7]

Systemic administration: Several studies and clinical trials have been carried out to show the efficiency of systemic administered tetracycline. Clinical studies on patients with localized aggressive periodontitis showed considerable resolution of tissue inflammation and increase in clinical attachment when treated with tetracycline in conjunction with RSI.[20,21] However, disease recurrence can take place in 25% of patients with localized aggressive periodontitis after receiving systemic tetracycline.[21] Clinical Study performed by Hellden showed no significant difference in the outcome of chronic periodontitis when treated with tetracycline in combination with RSI and when compared with RSI only.[22]

Local delivery: The purpose of local delivery of antibiotics is to achieve greater concentration of drug in periodontal pockets compared with systemic delivery.[7] Moreover, locally delivered antibiotics acts as bacteriocidal and can kill bacteria that are resistant to systemic antibiotics.[7] Actisite containing 12.7mg tetracycline-HCL and Atridox containing 10%doxycycline hyclate have been used for localized delivery. Multiple studies have shown positive effect in probing depth and clinical attachment gain when treated with Actisite or Atridox in combination with RSI.[23,24] Arestin is another drug consisting of 1mg minocycline and has also shown improvements in probing depth and attachment gain when used in conjunction with RSI.[25]

Penicillin/Augmentin: Penicillin is bactericidal against gram positive and gram negative bacteria and acts by inhibiting cell wall synthesis.[7,26] However, penicillin can

be ineffective against most bacteria in periodontal pockets as these bacteria produce β-Lactamase enzyme which destroy the β-Lactam ring of penicillin.[7] To overcome the resistance of bacteria, Augmentin was introduced which consist of amoxicillin and clavulanic acid. Clavulanic acid is a β-lactamase inhibitor and causes β-lactamase enzyme to bind to it instead of amoxicillin and thus making amoxicillin available for antimicrobial activity.[7] Clinical study by Magnusson on patients with refractory periodontitis showed 2mm of attachment gains and decrease in probing depths when treated with RSI and Augmentin.[27] However, use of Augmentin combined with mechanical plaque removal in chronic periodontitis did not demonstrate any additional positive results.[28]

Clindamycin: Clindamycin is bacteriostatic against gram positive and gram negative bacteria and acts by inhibiting protein synthesis.[7] However, certain bacteria like Aggregatibacter actinomycetemcomitans (Aa) and Eikenella corrondens can be resistant to clindamycin therefore making it ineffective in cases of aggressive periodontitis.[29,30] Study performed by Gordon in 1990 showed increased clinical attachments and decrease probing depths in patients with refractory periodontitis. Moreover, use of clindamycin may cause adverse effects including pseudomembranous colitis, thus clindamycin has a limited use in periodontal treatment.[7]

Metronidazole: Metronidazole is bactericidal against gram negative bacteria and acts by suppressing DNA synthesis of bacteria.[7] However, some bacteria like Fusobacterium and Aa may develop resistance.[31]

Systemic: Multiple studies have shown positive effects of metronidazole when used as adjunct to RSI. Studies performed by Winkelhoff and Gusberi showed increase in clinical attachment, decrease in probing depth and decrease bleeding on probing in patients with aggressive or refractory periodontitis.[32,33]

Local: Metronidazole can be delivered locally in periodontal pockets in the form of a gel called Elyzol consisting of 25% metronidazole benzoate. Gel may be administered in 2 visits one week apart. Griffiths performed a study on patients with chronic periodontitis using locally delivered metronidazole with RSI.[34] Study showed decrease in probing depths and increase attachment gains. However, another clinical study performed by Riep showed no significant difference over root surface instrumentation alone when patients with chronic periodontitis were treated with metronidazole gel in combination with RSI.[35]

Azithromycin: Azithromycin acts against gram positive as well as gram negative bacteria.[7] Generally, dosage of 250mg, once daily for 4 days may be given as this dosage can maintain concentration in periodontal tissues for up to 10 days.[7] Smith reported a clinical study in which 300mg of azithromycin daily for 3 days were given to patients with periodontal disease. Significant reduction in probing depths and reduced bleeding were charted after 22 weeks.[36] Moreover, azithromycin was given as an adjunct to RSI. However, more studies are required to evaluate the true efficacy of azithromycin in treatment of periodontal diseases.

ANTIBIOTICS IN SPECIFIC PERIODONTAL DISEASE

Chronic Periodontitis: It is a condition causing gingival inflammation, attachment loss and bone loss and is characterized by pocket formation and gingival recession.[3] Use of antibiotics in chronic periodontitis is not indicated as the pathogens in this condition can be poorly defined and may cause rapid recolonization following antibiotics.[16] Moreover, chronic periodontitis responds well following RSI.[37]

Aggressive Periodontitis: It can be either in localized or generalized form. Localized form can be characterized by bone and attachment loss around molars and/or incisors with no more than two teeth involved other than first molar and incisors, while generalized form is characterized by rapid bone loss and attachment loss interproximally involving at least three teeth other than first molar and incisors.[3] Traditionally, tetracycline 250mg, 4 times daily for 2 weeks was prescribed in combination with RSI.[16] However, due to tetracycline resistance of Aa, current regimen is metronidazole 375 or 400mg plus amoxicillin 250mg, 3 times daily for 1 week in combination with RSI.[16] This current regimen may result in 97% elimination of Aa.[16,38] Result of a study performed by Guerrero in 2005 on patients with generalized aggressive periodontitis showed improvements in probing depths and clinical attachment gains when treated with RSI combined with amoxicillin (500mg) and metronidazole (500mg), 3 times daily for 7 days.[39] On the other hand, different dentists have different regimen for antibiotics.[40] . (Table 2).

Acute Periodontal Abscess: It is characterized by collection of pus within the periodontal tissues.[3] Use of antibiotics may not be suggested in cases where the pus can be drained via RSI or incision.[16] However, when there is danger of systemic spreading of abscess or abscess is not drainable then amoxicillin 250mg or metronidazole 200mg, 3times daily for 5 days can be suggested.[16] Herrera performed a clinical study on patients with acute periodontal abscess in which one group received azythromycin (500mg, once daily for 3days), while other group received augmentin (500mg, 3times a day for 8 days).[41] Both groups showed significant resolution in abscess and improvement in probing depth with decrease pathogen count. Necrotizing Ulcerative Gingivitis and Periodontitis(NUG): Can be characterized by punched out papilla with pain and bleeding followed by pseudomembrane formation, while Necrotizing ulcerative periodontitis (NUP)

can be presented as NUG with infection spreading to ligaments and alveolar bone resulting in bone exposure.[3] After RSI, metronidazole 200mg, 3 times a day for 3 days can be prescribed.[16] Resistance of microorganisms against antibiotics: Approximately 7-11% of commonly used antibiotics are prescribed by dentists and improper use of antibiotics can lead to their resistance.[42] Moreover, resistant bacteria may pass from one individual to another via contact and other modes of transmission.[43] Bacteria and other pathogens are smart and they can acquire resistance against antibiotics.[42] Mechanism by which the bacteria can evade the effects of antibiotics are inactivation of enzymes, alteration of the receptor sites, limiting access to target sites, efflux of the drug from cells, preventing activation of drug or excessive production of target sites.[15,44]

Table 1: Modified and taken from Wiebe.[45] Adapted from 1999 International workshop for classification of periodontal diseases and conditions.[46]

Simplified Classification of periodontal diseases and conditions
I. Gingival Diseases
A. Dental plaque-induced gingival diseases
B. Non-plaque-induced gingival lesions
II. Chronic Periodontitis (Slight: 1-2 mm CAL; moderate: 3-4 mm CAL; severe: > 5 mm CAL)
A. Localized
B. Generalized (> 30% of sites are involved)
III. Aggressive Periodontitis (Slight: 1-2 mm CAL; moderate: 3-4 mm CAL; Severe: > 5 mm CAL)
A. Localized
B. Generalized (> 30% of sites are involved)
IV. Periodontitis as a Manifestation of Systemic Diseases
A. Associated with hematological disorders
B. Associated with genetic disorders
C. Not otherwise specified
V. Necrotizing Periodontal Diseases
A. Necrotizing ulcerative gingivitis
B. Necrotizing ulcerative periodontitis
VI. Abscesses of the Periodontium
A. Gingival abscess
B. Periodontal abscess
C. Pericoronal abscess
VII. Periodontitis Associated With Endodontic Lesions
A. Combined periodontic-endodontic lesions
VIII. Developmental or Acquired Deformities and Conditions
A. Localized tooth-related factors that modify or predispose to plaque-induced gingival diseases
B. Mucogingival deformities and conditions around teeth
C. Mucogingival deformities and conditions on edentulous ridges
D. Occlusal trauma

Table 2: Antibiotics regimen in periodontal diseases suggested by Walker [10] in 2002

No.	Antibiotic Name	Adult Dosage	Duration
1	Amoxicillin/ Augmentin	250mg or 500mg 3 times daily	10 days
2	Amoxicillin + Metronidazole	375mg or 400mg amoxillicin 3 times daily + 250mg Metronidazole 3 times daily	7 days
3	Clindamycin	300-150mg 4 times daily	14-10 days
4	Metronidazole	250mg 3 or 4 times daily	10 days
5	Tetracycline	250mg 4 times daily	21-14 days

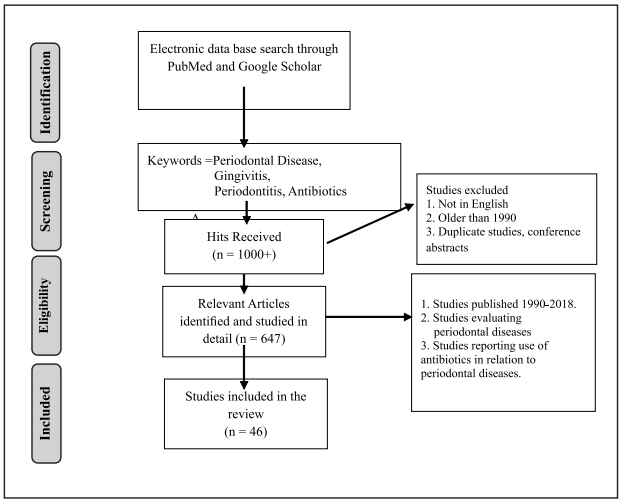

Fig 1: Flowchart showing identification, screening, and selection of studies for this review.

CONCLUSION

The main aim of periodontal therapy should be to eliminate or control the undesired effects of bacteria present in oral cavity in the form of biofilms. Therefore, mechanical instrumentation is required to physically disrupt the biofilms. Nevertheless, the bacteria have the tendency to re-colonize following mechanical therapy, therefore use of antibiotics can play a major role in the treatment of periodontal diseases. Use of antibiotics can be justified in cases with rapid signs and symptoms of destruction of periodontal tissues. Hence, antibiotics can be suggested in cases of aggressive periodontitis, periodontal abscess, necrotizing ulcerative gingivitis, necrotizing ulcerative periodontitis and periodontitis that do not respond well to RSI. However, antibiotics may cause side effects and the bacteria may develop resistance, therefore dentists should keep in mind the adverse effects and benefits while prescribing antibiotics. Moreover, antibiotics should always be given as an adjunct to RSI and oral hygiene

instructions to achieve successful outcome.

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Khabeer A:	Concept, Design and Proof reading
Alam BF:	Acquisition and critical review
Noreen S:	Analysis and interpretation of data
Faridi MA:	Data collection, Final approval
Ali S:	logical interpretation and presentation of the results

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

REVIEW ARTICLE

EFFICACY OF ROBOT-ASSISTED PHYSIOTHERAPY FOR PAIN MANAGEMENT IN NEUROLOGICAL DISORDERS: A SYSTEMATIC REVIEW

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ABSTRACT

Objective: Neurological disorders (ND) are ranked as the leading cause of death and disability around the globe and the escalating burden summons the advancements in the treatment strategies hence this systematic review aimed to fill the knowledge gap regarding the efficacy of robot-assisted physiotherapy (RAPT) for pain management in ND.

Materials and method: Scientific trials were sought by an extensive search via electronic databases mainly PubMed, PEDro and Scopus. Randomized controlled trials published from the year 2014 to April 2021, evaluating the potential effects of RAPT for pain management in ND were included in the review. The quality appraisal of the RCTs was analyzed via Cochrane tool for assessing risk of bias.

Results: The majority of the trials reported the effectiveness of RAPT using PARO robot, Armeo spring, Gloreha robot, and robotic Lokomat gait training system in significantly improving pain of ND such as stroke, dementia, phantom syndrome, and spinal cord injuries.

Conclusion: Large body of evidence suggested RAPT as a potential solution in improving pain of various ND. However, further rigorous trials are necessary to draw conclusive recommendations.

Keywords: Neurological disorders, pain, physiotherapy management, rehabilitation, robot-assisted physiotherapy, robotics

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INTRODUCTION

Neurological disorders (ND) are ranked as the second leading cause of death around the globe[1]. Among these disorders, stroke is the number one cause[2]. ND accounts for 6.3% of the global burden of diseases[3]. Furthermore, it is expected to raise, hence demands advancements in the treatment strategies.

Robotics is one of the most emerging gap areas in the neuro-rehabilitation panorama. Growing evidence claimed robot-assisted physiotherapy (RAPT) as a promising approach to provide feasible[4], accurate, repeatable, quantifiable, patient-centered therapy, while guaranteeing patient safety, speedy recovery, and unloading therapist workload as compared to traditional methods and also helps to maximize and maintain the therapy dose[5, 6, 7].

According to World Health Organization (WHO), ND are progressive and challenging health problem[8]. Scientific pieces of literatures reported pain as the common complaint of patients suffering from ND[9], greatly impacting the Quality Of Life (QOL)[10], also reduces patient adherence and treatment satisfaction[11]. Hence making the management of pain difficult[12]. Recently a multicenter experimental trial conducted by Aprile et al. concluded Robotic Therapy (RT) to be effective in reducing pain in stroke patients[13]. Well-documented researches show that robotic therapy utilizes various games that not only makes it interesting for the patients with ND but also allows them to be more independent, improve pain, QOL and promotes adherence to rehab program [14, 15]. Ample researches also claimed RT to be more effective than conventional therapy furthermore it is also reported to be cost effective[16, 17] and in improving cognitive function[18].

Previous systematic review and meta-analysis have reported RT to be effective in improving Activities of Daily Living (ADLs), motor control, and muscle strength of stroke survivors also identifies knowledge gaps in robotic rehabilitation[19-21].

It is noteworthy that despite the incredible effects of RAPT elucidated in the literature however in the field of neuro-rehabilitation the evidence regarding the efficacy of robotics for pain management in ND is still in infancy.

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Therefore, this systematic review (SR) is aimed to evaluate the efficacy of RAPT for pain management in ND.

MATERIAL & METHODS

Study Design: A SR was carried-out on Randomized Controlled Trials (RCTs) conducted on patients suffering from ND including stroke, dementia, spinal cord injury (SCI), and phantom- limb syndrome.

Review Protocol: The protocol for this SR is reported in consideration with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) recommendations[22].

Eligibility Criteria: Trials that met the following eligibility criteria were included:

1. Study design must be RCT.

2. Patients diagnosed with any type of ND, aged ≥ 18 years.

3. Studies addressing neuropathic pain as the main outcome measure.

4. RCTs published from 2014 to April 2021.

5. RCTs available in the English language.

Sources of information: Numerous electronic databases including PubMed, Scopus, PEDro, Web of Science, Cochrane Library, Scopus, and Med-line were scanned.

Search strategy: In January 2021, a systematic search was executed using various electronic databases in order to find out potentially eligible published trials. The key terms include (''Robotic therapy'' OR ''Robot-assisted physiotherapy '') AND (''neuropathic pain'' OR ''pain'') AND (''neurological disorders'' OR '' stroke'' OR ''spinal cord injury'' OR ''dementia'' OR ''phantom limb syndrome'' OR ''Parkinson'') AND (''physiotherapy'' OR "physical activity" OR'' exercise'' OR '' neurological rehabilitation'') AND (''RCT'' OR '' randomized controlled trial'') AND '' custom date range (2014 to 2021)". Moreover additional trials were extracted using the reference list of the included RCTs. Initially the titles and/or abstracts were assessed for eligibility and trials not meeting the criteria for eligibility were excluded. However, the eligible trials were rigorously reviewed in full to appraise the credibility in consideration with the PRISMA recommendations.

Trials Selection: Initial filtration of articles was done based on the titles and/or abstracts also investigated against the inclusion criteria of the SR. Total 132 trials were pooled-out by the primary search. Out of these, some trials were irrelevant, others full-text were not accessible, replicated or having the poor methodological quality or not available in the English language. However eight potential trials addressing the efficacy of RAPT for pain management in different ND were included in this SR. The disagreements regarding the trials were resolved after a combined discussion of all the authors.

Extraction of Data: The data such as principle author name, trial publication year, the population of the study, sample size, treatment applied, and the main findings of the trial were extracted from the selected trials.

Risk of Bias: Critical appraisal of the trials was carried-out for evaluating the methodological quality by using the Cochrane tool for assessing risk of bias[23]. This tool assesses the biases in various domains which includes random allocation, allocation concealment, blinding of participants and outcome assessment, incomplete outcome data, selective reporting and other bias.

RESULTS

Selection of studies: A total 132 trials were retrieved after the initial systematic search through different databases. However 115 articles were excluded based on titles, objectives and replication, remaining 17 full-text RCTs were reviewed, of which eight potential trials[24-31] were included in this SR. The selection strategy of the trials is shown in the PRISMA flow diagram (Figure 1).

Characteristics of Studies: Total RCTs included in this review involve 242 neurological patients suffering from stroke, dementia, phantom upper limb syndrome, and SCI. The included trials were conducted from December 2014 to September 2020. Few trials reported sample size calculation. The total follow-up periods of the studies ranges from three weeks to one and half months. Different outcomes measures were used i.e. NPRS, VAS, NRPS, and PAINAD[24-31] (Table 1).

Abbreviations: Exercises (Ex's), Joint Mobilization Technique (JMT), Passive Range Of Motion (PROM), Random Training (RT), Conventional Physiotherapy (CPT), Upper Extremity (UE), Experimental Group (EG), Control Group (CG), Robotic Therapy (RT), Spinal Cord Injury (SCI), Strength Training (ST), Robotic Assisted Gait Training (RGAT), Adduction (Add), Abduction (Abd), Flexion (Flex) and Extension (Ext).

Results of the studies related to the evaluation of pain in neurological patients: Pu Lihui et al. conducted various trials [24, 25, 27] on dementia patients using PARO robot and reported a significant decrease in pain in all studies. Another research conducted by Taveggia G et al. [30] in Italy compared Armeo spring robotic device versus traditional physiotherapy results revealed more improvement in pain in patients receiving Armeo spring robotic therapy. Similarly, the pain had also decreased significantly in post-stroke hemiplegic shoulder patients receiving Gloreha RT along with passive ROM and stretching ex's [29]. The majority of the trials reported improvement in pain in different ND using RAPT [24-31]. No study documented any side effects of the use of robot.

Table 2. Cochrane summary of the risk of bias Indications: High risk of bias (-), low risk of bias (+) and unclear risk of bias (?), Higgins et al. [23].

Risk of bias within trials and quality appraisal: All the selected trials had a low risk of bias in random allocation [24-31]. Six of the trials showed a high risk of biasness in allocation concealment,[24-28, 31] however only one trial showed a low risk of bias[29]. The majority of the studies didn't show participant blinding[24-27, 31] but the studies by Kim MS et al. [28], Villafane et al. [29] and Taveggia et al.[30] reported participant blinding. All the trials showed a low risk of bias in selective reporting, except Kim et al. [28]. The risk of bias could not be determined because of the poor methodological quality of a few studies[30-31] (Table 2).

Table 1: Synopsis of the trials related to the efficacy of RAPT for pain management in ND

Authors	Pu Lihui et al. 24	Pu Lihui et al.25	Yanagi et al.26	Pu Lihui et al.27	Kim et al.28	Villafane et al.29	Taveggia et al.30	Labruyère et al. 31
Year	2020	2020	2020	2019	2019	2018	2016	2014
Study Population	Dementia	Dementia	Phantom syndrome	Dementia	Stroke	Stroke	Stroke	Incomplete SCI
Sample size	n=43	n=43	n=12	n=11	n=38	n=32	n=54	n=9
Intervention	EG= Received PARO RT (A baby harp robot that rehabilitates using its four senses sight, hearing, balance, tactile sense and talk with user also CG= Usual care activity (singing, story and music listening) 30 mins session, 5 days/wk. Total 30 sessions	EG=PARO RT CG= Usual care activity (singing, story and music listening) 30 mins session, 5 days/wk. Total 30 sessions	EG=Assigned real training. CG=Assigned RT MEG signals were recorded when different phantom hand movements were performed. Real training includes 400 ms virtual training and in RT 200 ms virtual images were controlled. Total 28 sessions	EG= PARO RT CG= Usual care 30 mins session, 5 days/wk. Total 30 sessions	Bobath approach and physical modalities were given to both the gps. EG= Robot-assisted shoulder JMT and stretching ex's CG= PROM ex's 30 mins session, 5 days/wk. Total 20 sessions	Both groups received CPT including assisted stretching, shoulder and arm ex's and functional reaching task. EG= Received additional passive mobilization of hand through Gloreha 30 mins session, 3 days/wk. Total 9 sessions	EG= Armeo spring robotic UE movement + postural correction + CPT (active-assisted and passive mobilization of UE based on bobath concept). 5xd/wk. CG= CPT 30 mins session 5 days/wk. Total 30 sessions	EG=R-GAT-ST CG=ST-RGAT RGAT is controlled via Lokomat system in which virtual gait training was done. ST including isotonic leg press in supine position and isotonic hip add, abd, flex and ext. 45 mins session, 4 days/wk. Total 16 sessions
Main finding	PARO RT reduces chronic pain	Significant ↓ in pain observes in EG as compared to CG	Pain significantly reduced via real training	EG reported significant ↓ in pain	EG had shown significant ↓ in pain	RT is more effective in treating post stroke shoulder pain	Both gps reported significant ↓ in pain however, EG shows more improvement	Pain ↓ in both groups

Table 2: Table 2. Cochrane summary of the risk of bias

Randomised Controlled Trial	Random Allocation	Allocation Concealment	Participants Blinding	Outcome Assessment Blinding	Incomplete Outcome Data	Selective Reporting	Other Bias
Pu Lihui et al.24	+	_	_	_	+	+	+
Pu Lihui et al.25	+	_	_	_	+	+	+
Yanagisawa et al.26	+	_	_	+	+	+	+
Pu Lihui et al.27	+	_	_	_	+	+	+
Kim et al.28	+	_	+	_	+	_	+
Villafane et al.29	+	?	+	+	+	+	+
Taveggia et al.30	+	+	+	+	+	+	?
Labruyere et al. 31	+	_	_	+	+	+	?

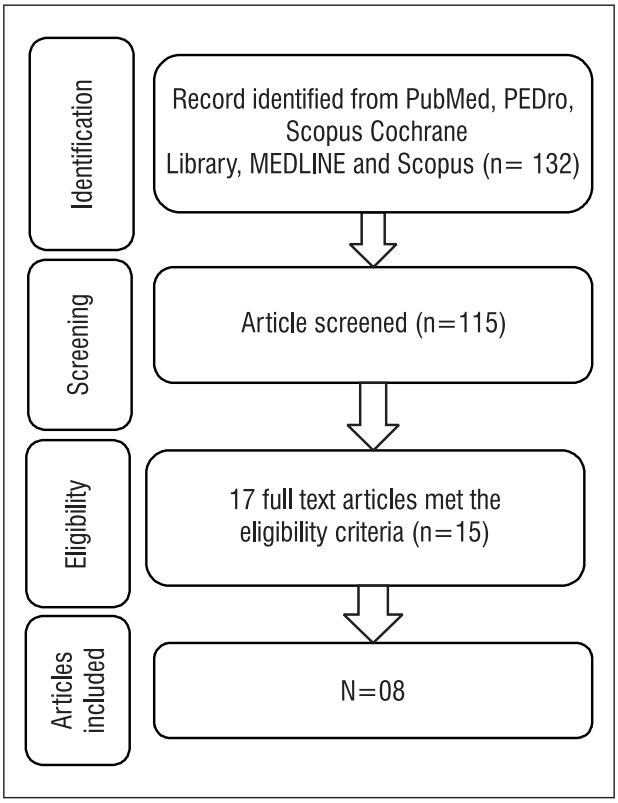

Figure 1. Trials selection strategy

Synthesis of results: The majority of the trials reported the effectiveness of RAPT using PARO robot, Armeo spring, Gloreha robot and robotic Lokomat gait training system in significantly improving the pain of various ND such as stroke, dementia, phantom syndrome and SCI.

DISCUSSION

This comprehensive review is the first to address the knowledge gap regarding the efficacy of RAPT for pain management in ND by rigorously scanning the latest RCTs conducted over the past 8 years. This SR examines eight quality trials including, 242 neurological patients suffering from stroke, dementia, phantom upper limb syndrome, and incomplete SCI.

A fascinating study by Villafane JH et al.[29] reported RAPT to be more effective than Conventional Physiotherapy (CPT) alone. However, these findings are contradicted by a recent (2021) case-control study conducted in Italy by Paolucci et al. [32], which suggested that robot-assisted rehabilitation and CPT both are equally effective in reducing pain in chronic stroke patients. Similarly, another study by Abdullah et al. also reported no significant difference[33].

The current SR mainly highlights the role of robotics for pain management. However a previous, meta-analysis published by Rachele Bertani et al.[34] documented RT effectiveness in the recovery of upper limb motor function specifically in stroke patients. The same findings were observed by Fernanda et al.[35] with emphasis that RT is not only effective in motor function improvement but also in enhancing the strength of muscles in the same population. Nirit Geva et al.[36] added that RT is also effective in improving the moods of patients. However, these researches claimed the lack of quality data availability.

It is noteworthy that the findings of this review are in line with the studies conducted by Ach et al.[37], Cruciger et al.[38] and Stampacchia et al.[39] which further endorsed the imperative role of RT in the reduction of neurological pain. However, Remi et al.[40] claimed no significant pain reduction in stroke patients after RT.

This review is the first to elucidate an up-to-date finding regarding the emerging role of RAPT in neurological pain management and addresses major health implications however some potential limitations associated with this review include few numbers of trials with a small sample size. Furthermore, a variety of robotic therapies were categorized under the term RAPT.

As the blooming role of robotics in neurological rehabilitation still lies in its infancy, therefore a robust and reliable conclusion cannot be drawn. Hence, it is recommended that further quality trials with large sample size and long follow up duration addressing dose-response of different robotic therapies and patients independent handling is the need of time to explore precise effects of this innovative treatment strategy.

CONCLUSION

A large body of evidence supports the effectiveness of RAPT for improving pain in various ND such as stroke, dementia, phantom syndrome, and SCI. However due to scarcity of the evidence on robotic rehabilitation, a reliable and robust conclusion cannot be drawn. Further high quality, rigorous, multi-center, and large-scale trials are necessary to draw conclusive recommendations.

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Shaikh HA: Planning, manuscript writing, formatting and critical review

Waheed N: Manuscript writing and critical review

Zaidi SWR: Data searching, manuscript writing and critical review

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

DIFFUSE UTERINE LEIOMYOMATOSIS (DUL) COEXISTENT WITH INTRA-VASCULAR LEIOMYOMATOSIS MASQUERADING AS AN ENDOMETRIAL STROMAL TUMOR: A REPORT OF AN EXTREMELY RARE CASE

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ABSTRACT

Case Report: We present a 38 year old female with coexistent diffuse leiomyomatosis as well as intravascular leiomyomatosis of the uterus masquerading as an endometrial stromal tumor. A strong positivity for Desmin and Progesterone receptor (PR) favoured DUL while negative immunoreactivity for CD-10 helped in excluding endometrial stromal tumor.

Conclusion: DUL is a distinct entity from the uterine leiomyomas in terms of varied gross and microscopic features. To the best of our knowledge, this is the first report of coexistence of two rare variants of leiomyoma- diffuse and intravascular leiomyomatosis.

Keywords: diffuse uterine leiomyomatosis, leiomyoma, endometrial stromal tumor

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INTRODUCTION

Diffuse uterine leiomyomatosis (DUL) also referred to as complete fibromyomatosis, myomatosis, diffusemyomatous tendency is a rare condition characterized by symmetric enlargement of the uterus due to numerous poorly defined, confluent nodules almost completely replacing the myometrium.[1]

Baschinsky et al[2] have proposed that diffuse leiomyomatosis of the uterus is an exaggerated proliferation of multiple leiomyomas budding into each other and merging imperceptibly so that discrete nodules could not be readily noticeable by gross examination. Intravascular leiomymatosis (IVL) is a rare variant of leiomyoma characterised by smooth muscle proliferation within the lumen of blood vessel with attachment to the vessel walls.[3]

The clinical presentation of DUL is indistinguishable from uterine leiomyomas with patients usually presenting with abdominal pain, abnormal uterine bleeding or infertility. Although microscopic features of leiomyomatosis include haphazardly arranged fascicles of smooth muscle cells, it may exhibit a histological overlap with multiple leiomyomas andendometrial stromal sarcoma thereby posing a diagnostic challenge to the pathologist.[4,6] To the best of our knowledge, we present the first report of coexistent diffuse and intravascular leiomyomatosis, mascerading as an endometrial stromal tumor.

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CASE REPORT

A 38-year-old woman (gravida 2, para 2) presented to the Gynaecology clinic with abnormal uterine bleeding, dysmenorrhea and pelvic pain for last 6-8 months. Complete blood count revealed haemoglobin 10 g%, total leucocyte count 8,500/µl with differential leucocyte count within normal limits, platelets 1.6 lacs/µl and erythrocyte sedimentation rate of 12mm/hr.

Biochemical investigations were within the normal reference range. Pelvic ultrasound revealed a symmetrically enlarged uterus measuring 13x10x6 cm with multiple intramural fibroids, smallest being 0.5 cm while large discernable one was 3.5cm in diameter. Total abdominal hysterectomy with bilateral salpingo-oophorectomy was performed.

Grossly, uterus was uniformly enlarged and on serial sectioning had a multinodular appearance due to almost complete replacement of myometrium by many intramural and subserosal nodules coalescing into each

other. Cut surface of nodules was greyish white with a whorled/ trabeculated appearance. The other pelvic organs, parametrium and ovaries were normal. Histologically, the nodules were composed of interlacing bundles of smooth muscle cells which had multifocal areas of hyalinization and degeneration (Figure 1). The nodules blended with each other and amalgamated imperceptibly with the surrounding normal myometrium. Proliferating small vessels resembling the endometrial spiral arterioles were observed, and there were bands of hyaline connective tissue separating islands and clusters of bland neoplastic stromal cells similar to ESS (figure 2). No cellular pleomorphism or abnormal mitotic figures were noted. Immunohistochemistry revealed strong positivity for smooth muscle actin (SMA), desmin, progesterone receptor-PR (figure 2) and a 3-5% Ki-67 labelling index.

A negative immunoreactivity for CD-10 helped in excluding endometrial stromal tumor. Extensive sampling was done which revealed focal areas where a proportion of the fibroid was seen within blood vessels at places attached to their walls. So, a final diagnosis of diffuse leiomyomatosis with a component of intravascular leiomyomatosis was rendered.

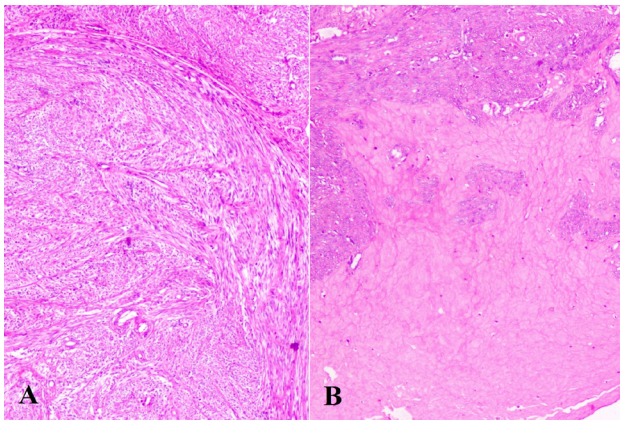

Fig 1: Photomicrograph showing A)the tumor nodules composed of interlacing bundles of smooth muscle cells, B) Areas of hyalinization and degeneration (H&E, 200X)

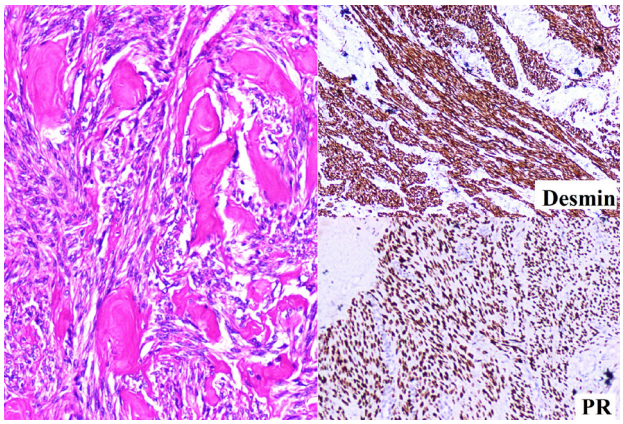

Fig 2: Photomicrograph showing bands of hyaline connective tissue separating islands and clusters of bland neoplastic stromal cells similar to ESS (H&E, 400X), Immunohistochemistry for desmin and PR showed strong positivity.

DISCUSSION

Diffuse uterine leiomyomatosis is a benign, extremely unusual condition with uniform enlargement of the uterus on account of nearly complete replacement of the myometrium by many poorly defined leiomyomatous nodules coalescing into each other.[1] Intravascular leiomymatosis is another rare variant of leiomyoma characterised by smooth muscle proliferation within the lumen of blood vessel with attachment to the vessel walls.[3]

Leiomyomas are clonal neoplasms with consistent cytogenetic alterations. It is postulated that various tumors within the diffuse uterine leiomyomatosis arise from different clones, implying that DUL may be an exuberant growth of multiple uterine leiomyomas budding into each other and blending imperceptibly so that it becomes difficult to separately identify individual nodules grossly.[2]

The most common presentation of DUL patient is abdominal pain and abnormal uterine bleeding which is akin to most uterine leiomyomas.[1] Patients usually belong to third and fourth decades of life with complaints of menorrhagia, dysmenorrhea, infertility, and pelvic pressure.[2,5] Several authors have reported cases of DUL with coexistent pregnancy, although complications like premature rupture of membranes, cervical incompetence, intrapartum haemorrhage necessitating hysterectomy have been documented. [7,8] Few cases of benign metastasizing leiomyomatosis have also been reported in the literature.[9]

The characteristic histopathology of DUL reveals nodules blending with each other as well as moulding inseparably with the surrounding myometrium. The nodules comprise of benign smooth muscle cells in compact fascicles and interweaving bundles. Histologically, the differential diagnosis of leiomyomatosis includes multiple leiomyomas, intravascular leiomyomatosis and endometrial stromal sarcoma (ESS).[1,2,4,5]

Uniform symmetrical involvement of the entire myometrium by smooth muscle nodules without well-defined borders between the nodules favours DUL while multiple leiomyomas are well circumscribed with asymmetrical involvement of the uterus.[2,5] Endometrial stromal sarcoma is characterized by its invasive growth with a clear cut transition with the normal myometrium, and a sheet like arrangement unlike DUL which shows a fascicular growth pattern. Moreover, microscopically ESS has small tumor cells with round to oval nuclei and scant cytoplasm separating the thick walled vessels and intravascular growth.[5,6] Immunohistoreactivity for CD-10 favours ESS over DUL. Salient features of intravascular leiomyomatosis include a creamy to yellowish colour grossly with intravas-

cular extensions of wormlike smooth muscle tumor with multinodular indistinct margins and the presence of some or all of the neoplastic smooth muscle within the vascular channels, microscopically as was observed in the present case.

Nisolle et al[10] concluded that diffuse leiomyomatosis lesions may be under the influence of progesterone as progesterone receptors (PRs) were significantly higher in leiomyoma than in the adjacent myometrium similar to our case. Antiprogestin agents may serve as alternative mode of treatment DUL.

Two theories have been proposed for the occurrence of intravascular leiomyomatosis- primary growth within the vessel or an extension of pre-existing leiomyomas. The definitive treatment of IVL includes total hysterectomy with possible oophorectomy and removal of tumors from within venous and cardiac systems. GnRH analogues and anti-estrogens may be used as a conservative approach.[11]

The treatment of choice still remains hysterectomy, even though the patients are young in the third or fourth decades of life, as the numerous confluent nodules are not amenable to myomectomy. No recurrences have been reported following hysterectomy for DUL. Various treatment modalities like uterine arterial embolization, GnRH analogues, hysteroscopic resection for early-stage diffuse uterine leiomyomatosis have been proposed as an alternative to hysterectomy for the treatment of DUL.[6]

To conclude, diffuse uterine leiomyomatosis is a clinically distinct entity from the uterine leiomyomas in terms of varied gross and microscopic features as well as possibly pathogenesis and their treatment. DUL may on occasion be diagnostically challenging for the pathologists.

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

6 Conflict of interest

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

7 Confidentiality

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

8 Correction and retraction of articles

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

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

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

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

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

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

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

9 Correspondence

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

10 Fee submission process

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

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

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

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

11 Roles of editorial board, editors and members

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

11.1: The roles of the Editorial Board are:

11.1.1: To offer expertise in their specialist area

11.1.2: To review submitted manuscripts

11.1.3: To advise on journal policy and scope

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

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

11.1.6: To attract new and established authors and articles

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

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

11.2: The Patron:

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

11.3: The Chief Editor:

11.3.1: The criteria for selection of Chief Editor are:

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

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

iii. Being a reviewer for an international peer reviewed journal

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

v. Enthusiasm to undertake the Editor role

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

11.3.2: The roles of Chief Editor are:

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

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

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

11.3.3: Managing editor:

The roles of manging editor are:

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

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

iii. To regularly evaluate the research work

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

11.3.4: Executive editor:

The roles of executive editor are:

i. To evaluate the research articles presented for publication

ii. To help the editorial board in policy making

iii. The help the editorial board in smooth publishing

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

11.3.5: Section editors:

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

i. Bibliography

ii. Proof-reading

iii. Academic writing reviewing, grammar and spell checking

iv. Dissemination of articles for review

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

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

vii. others

11.3.5: Editorial advisory board:

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

12. POLICY REGARDING RECRUITMENT AND CONTINUATION OF EDITORIAL BOARD

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

13. Plagiarism policy

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

14 Contact information

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

REFERENCES

1. ICMJE recommendations

2. COPE guidelines

3. SCOPUS

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

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