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EDITORIAL

Science Communication: An essential skill for clinicians

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Keywords: *Science journalism, clinical education, core competencies, professional development.*

While growing up in the digital age, most of us had the opportunity to witness the development of advanced methods and means of communication. We can fondly remember shifting from searching months' old manuscripts in the libraries to using a smartphone to easily access the latest science in the palm of our hands. This development has not been confined to the scientific manuscripts only. Internet and social media platforms gave an opportunity to any individual interested in any field to develop ideas and share them with a wider audience. This freedom, coupled with the trend of covering medico-scientific news in the electronic and print media has made the general public more concerned about their physical and mental health. However, unfortunately, these developments have not all been very fruitful. In a real world setting where opinions are stronger than the truth, opportunists managed to exploit it to publicize their sociopolitical agenda.[1] Advertisement of quackery, opposition of vaccination drives and defaming of safe surgical procedures have risen to prominence over the recent decades.[2] These individuals and organized groups generally back their claims with unregulated blogs and fake news websites for spreading pseudoscience.

The spread of such misinformation is prevalent throughout the world. Pakistan, hence, is no exception. Being the 6th most populous country with more than 90% individuals not having a single degree, the medico-scientific illiteracy gains all the more importance.[3] Moreover, a religiously and medically pluralistic society with a weak health management system further empowers the miscreants to strengthen their own agenda. The major contributing factor for the spread of such misinformation is the vacuum created by the lack of trained science communicators and journalists with a background in clinical sciences.[4] Though advanced research is being carried out at many centers in Pakistan in biomedical and clinical sciences as well as in clinical practice yet its communication to the general masses is negligible. Researchers are focused on reporting their findings to high impact journals that are meant to be read by their colleagues and fellow specialists. Furthermore, even the access to these journals is afforded by only some institutes and that too at a very expensive price. This lack of relatability makes a common man rely on the resources and clinical advice that is often misleading, damaging and, sometimes, even lethal.

Clinicians and biomedical scientists are socially accountable to develop and promote practices that ensure active community engagement. Communicating science in a manner that is easily interpretable by the general public can be quite advantageous. Firstly, patients would have access to the accurate information from an authentic source.[5] This can significantly decrease the incidence of self-medication, thereby, improving the medication compliance and therapeutic outcomes. Moreover, the clinicians and the academia can capitalize the opportunity as it is a known fact that funding drives science. All national and international entities, generously fund projects that ensure the transfer of benefits to the masses. Science communication can, hence, ensure a persuasive public call-to-action drive.

For effective science communication, the local socio-political perspective shall be taken into account. With a high degree of illiteracy, let alone scientific misinterpretation, the clinicians and biomedical scientists shall make an effort to understand the demands of the local community. Addressing these demands through intelligent storytelling can enhance the acceptance of science. A sense of accessibility, clarity and honesty shall prevail throughout the scientific communication process. Though the scientific manuscripts encourage the provision of the minutest of all the details, while communicating science to the masses a broader picture has to be developed and delivered.[6] The target audience should be communicated as to how is the study relevant to them in a digestible yet scientifically credible manner. In order to develop responsible science communication in the country, adequate training modules shall be included in the curriculum, both at undergraduate and post-graduate levels. This ensures that the trainees develop themselves as critical thinkers and communicators. Moreover, the academia, clinicians and trainees shall all ensure their active presence on the social media platforms. Establishment of communication and advancement departments in the institutes of higher learning can especially be helpful.

In conclusion, it is imperative to challenge the deceitful propaganda of multiple sociopolitical entities through effective scientific communication and journalism. Appropriate training and research in the field can help in harnessing the potential of younger generation of clinicians to be effective communicators and empathic decision makers. Efforts directed at developing the mindset of having a good societal impact, rather than having a good impact factor only, can be beneficial in developing good scientists and clinicians.

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ORIGINAL ARTICLE

Diagnostic accuracy of ultrasound in detection of pregnancy associated breast cancer

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Author`s Contribution

[1] Data analysis and interpretation of data drafting
[2] Conception design and interpretation of data revising
[3] Analysis of data drafting of article, final approval
[4] Conception and design, revising it critically for important intellectual content

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A B S T R A C T

Introduction: Some unique physiological changes occur in breast volume and water content during pregnancy which makes the radiological evaluation of the breast difficult. As a result, diagnosis of Pregnancy Associated Breast Cancer. is often delayed.

Objective: To find out the diagnostic accuracy of ultrasonography in detection of pregnancy associated breast cancer taking histopathology as gold standard.

Methodology: Present cross-sectional study was carried out at the Department of Diagnostic Radiology of INMOL Hospital, Lahore. Ultrasound of 200 women was performed using the equipment Toshiba Aplio 500. Before the examination, patient was explained about the procedure.

The patient was laid supine and then turned slightly in oblique position to scan the breast with high frequency linear probe (7.5-10 MHz). The contra-lateral breast and both axillae were also scanned in the same way. Findings were categorized on the basis of Breast Imaging Reporting and Data System (BI-RADS) assessment categories. Subsequently the breast tissue was sent to histopathology laboratory for tissue diagnosis. The pathologist was blinded of the results of ultrasonography.

Results: Mean age was 34 ± 11.36 years. Twenty-eight percent patients were primi-para while 72% patients were multi-para. Diagnostic accuracy of ultrasonography taking histopathology as gold standard was analyzed and ultrasonography had sensitivity 84.78%, specificity 98.05%, positive predictive value 92.85%, negative predictive value 95.56% and diagnostic accuracy was 95%. Invasive ductal carcinoma was most commonly observed (P<0.001) malignant histopathology. On the other hand, significantly high (P = 0.033) number of benign lesions were Fibroadenomas.

Conclusion: The high sensitivity and specificity along with easy availability, and non-invasive nature makes ultrasonography a very useful technique for the diagnosis of Pregnancy Associated Breast Cancer.

Keywords: *Diagnostic accuracy, ultrasonography, pregnancy associated breast cancer, histopathology.*

Introduction

Pregnancy associated breast cancer (PABC) refers to the breast cancer which is diagnosed during pregnancy or in the first 12 months' post-partum, or at any time during lactation. Incidence of PABC is about 300 per million pregnancies. Approximately, 0.2 - 2.5% of all breast cancers are linked with pregnancy.[1-3]

As childbearing trends are greatly changing and most of the women in recent times delay childbearing until their 30s or 40s.The incidence of PABC may show drastic increase, since old age is already a known risk factor for breast cancer. So, the proper workup of breast related complaints during pregnancy and lactation is becoming increasingly important.[4]

During pregnancy, some unique physiological changes occur in breast volume and water content which make the radiological evaluation of the breast difficult. These underlying changes in breast tissue and the use of imaging with ionizing radiations which is contraindicated during pregnancy may result in delayed detection of PABC. A non-invasive test is required in these situations.[5] Ultrasonography is considered to be the first-line modality in evaluation of a palpable breast mass during pregnancy or lactation.[1, 6]

This study aims to determine the accuracy of ultrasound in detecting breast malignancy in pregnant and lactating women of this region as there is scarcity of local data in this regard. This study might prove to be useful in establishing the role of ultrasound in early detection of pregnancy associated breast cancer as ultrasound is an easy, affordable and non-invasive radiological investigation.

Methodology

The present cross-sectional study was conducted at the Department of Diagnostic Radiology, of INMOL Hospital, Lahore during June -December 2019. Sample size was calculated by using sensitivity & specificity sample size calculator (open epi.com) taking sensitivity of the test as 57% with 15% margin of error. Specificity of the test as 81.8% with 85% margins of error and expected prevalence as 14.9%.[4] Confidence level was set to 95% and precision required was adjusted to 10%. The sample size calculated came out to be 200. Non-probability consecutive sampling technique was used.

Pregnant or lactating women presenting with symptomatic breast (symptoms may include any or all of the following i.e. palpable lump, pain, skin or nipple retraction, nipple discharge) aged between 18-45 years were included. Patients with prior history of breast cancer and patients who were not willing to participate in the study were excluded.

Permission and approval of the study was sought from the hospital ethics committee for conducting the study. Patients were enrolled as per inclusion criteria with prior informed written consent. Ultrasound was performed using the equipment Toshiba Aplio 500. The patient was explained about procedure prior to the examination. The patient was laid supine, arm raised and placed under the head to keep the breast firm on to the chest wall and then turned slightly in oblique position to scan the breast with high frequency linear probe (7.5-10 MHz). The contra-lateral breast and both axillae were also scanned in the same way. Findings were categorized on the basis of Breast Imaging Reporting and Data System (BI-RADS) assessment categories. BI-RADS category 1 to 3 was labelled as negative for malignancy whereas category 4 and above was labelled as positive for breast cancer (Figure 2 & 3).

Subsequently the breast tissue was sent to histopathology laboratory for tissue diagnosis. Breast tissue which was labelled as benign on histopathology was taken as negative for breast cancer, whereas breast tissue having atypical or malignant cells was taken as positive for breast cancer on histopathology. The pathologist was blinded of the results of ultrasonography. All the gathered information was entered in the proforma.

Data were entered in SPSS version 20. Quantitative variables like age was measured as mean ± SD. Qualitative variables like symptoms, positive/negative on ultrasound and histopathology was measured as frequency and percentages. A 2×2 Table was constructed to determine the sensitivity, specificity, PPV, NPV and accuracy of ultrasound. Effect modifiers like age, parity, tumour size, BMI were controlled by stratification. Post stratification diagnostic accuracy was measured. Chi square test was applied for the determination of significance in categorical variables. P <0.05 was considered significant.

Results

Mean age was 34 years with SD ± 11.36. Parity distribution among 200 patients showed that 56 (28%) patients were primi-para while 144 (72%) patients were multi-para and 116 (58%) patients had tumor size >2 cm (Table 1). Status of obesity among 200 patients was analyzed as 90 (45%) patients were non obese while 110

(55%) patients were obese. Patient characteristics are described in Table 1.

Table 1: Patient characteristics

Variable	Subgroup	Frequency (%)
Age	18-30 years	76 (38%)
	31-45 years	124 (62%)
Mean age: 34.0 ± 11.36 (18-45) years		
Parity distribution	Primi para	56 (28%)
	Multi para	144 (72%)
Tumor size	≤ 2 cm	84 (42%)
	>2 cm	116 (58%)
Mean tumor size: 2.0 ± 1.82 cm		
Obesity	Non obese	90 (45%)
	Obese	110 (55%)

Ultrasonography findings for breast cancer among the patients were positive in 42 (21.0%) patients and were negative in 158 (79.0%) patients (Figure 1).

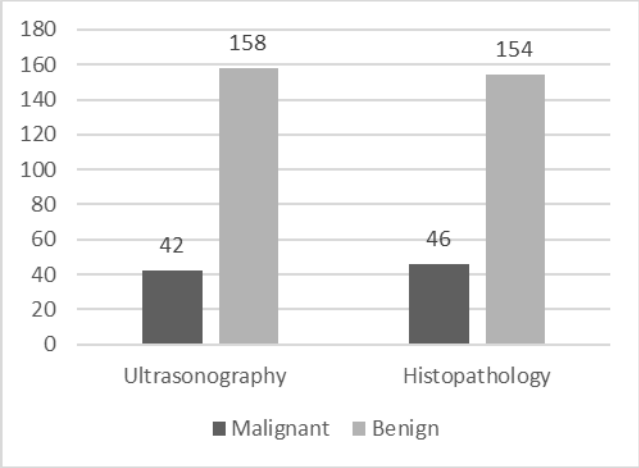

Figure 1: Comparison of ultrasonographic findings with histopathology for differentiating benign and malignant lesions.

Ultra-sonographic features of the patients with PABC histopathologically diagnosed with Invasive ductal carcinoma are shown in Figure 2 & 3. Histopathology was performed for all the patients. Histopathology findings among 200 patients were analyzed and breast cancer was positive in 46 (23.0%) and negative in 154 (77.0%) patients (Figure 1). Out of 42 patients with positive Ultrasonography Findings 3 had negative histopathology results depicting false positivity (Table 2). On the other hands 7 patients with negative ultra-sonographic findings had positive histopathology i.e., false negative (Table 2).

Table 2: Breast Cancer Histopathology Vs Ultrasonography Findings (n=200)

Ultrasonography	Histopathology		
	Positive	Negative	Total
Positive	39	3	42 (21%)
Negative	7	151	158 (79%)
Total	46 (23%)	154 (77%)	200

In malignant patients, Invasive ductal carcinoma (IDC) was the significantly high histological type (P<0.001). It was observed in 39 out of 42 cases (92.85%). Two (4.76%) patients were diagnosed with Invasive Lobular Carcinoma (ILC) and one (2.38%) had medullary carcinoma.

On the other hand, benign lesions (n=158) were predominantly Fibro adenomas i.e., 43 (27.2%) followed by Mastitis/Abscess in 37 (23.4%) and Galactocele in 31(19.6%) patients. Lactating adenomas were seen in 28 (17.7%) and Fibrocystic changes were observed in 19 (12.0%) patients. Statistically significant difference was observed in the presentation of benign lesions too, with P=0.033 applying chi square test.

Diagnostic accuracy of ultrasonography taking histopathology as gold standard was analyzed. Ultrasonography had sensitivity of 84.78%, specificity 98.05%, positive predictive value 92.85%, negative predictive value 95.56% and diagnostic accuracy was 95%. Stratification of diagnostic accuracy of ultrasonography taking histopathology as gold standard was done with respect to age, parity, tumor size and obesity.

Patients were stratified into two groups i.e., 18-30 Years (n=76) and 31-45 years (n=124) with respect to age. It was observed that ultra-sonographic findings were consistent with respect to age. In the patient group 18-30 years, sensitivity, specificity, PPV, NPV and diagnostic accuracy were 83.35, 96.42, 87.5, 95.0 and 93.42% respectively. It was 82.75, 97.89, 92.30, 94.89 and 94.35% respectively in the patients ranging between 31-45 years. Similar observations were made in Primi para and multi para women. In primi para (n= 56), sensitivity of ultrasound was 84.61 vs. 84.84% in multi para in diagnosing PABC. Specificity of the modality was 97.67 vs. 98.19%, PPV remained 91.66 and 93.33% while, NPV and diagnostic accuracy were 95.45 vs. 95.61% and

94.64 vs. 95.13% respectively in both prima para and multi para patients.

Tumor size ≤2 cm (n=84) and >2cm (n=116) was also compared for the determination of any potential difference in diagnostic efficiency of ultrasound in diagnosing PABC. Sensitivity was 84.21 vs. 84.84%, specificity was found to be 96.92 vs. 97.75%, PPV was 88.88 and 91.66%, NPV 95.45 vs. 94.56% and diagnostic accuracy was 94.04 and 93.96% with respect to the tumor size <2 cm and >2 cm respectively.

In non-obese (n=90) and obese (n=110) women, the sensitivity of ultrasound was 80.95 vs. 84.0%, specificity was 97.10 and 97.64%, PPV and NPV were 89.47 vs. 91.30% and 94.36 and 95.40% respectively. Diagnostic accuracy was 93.33 and 94.54% in both non obese and non-obese women respectively. The study shows comparable sensitivity, specificity, PPV, NPV and diagnostic accuracy of ultrasound with respect to above mentioned factors.

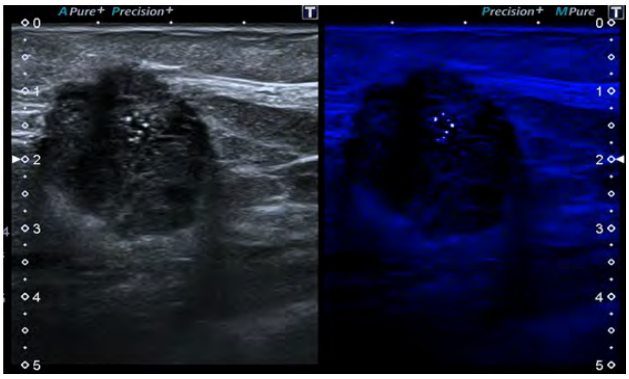

Figure 2: Pregnancy-associated breast cancer in a 34-year-old lactating woman, 7 months' post-partum, presented with a palpable mass in the left breast. Ultrasonography showed an irregular-shaped, hypoechoic mass at 12 0' clock position in left breast with micro lobulated margins and micro calcifications within the mass. Core needle biopsy revealed invasive ductal carcinoma. The patient received neoadjuvant chemotherapy followed by breast-conserving surgery.

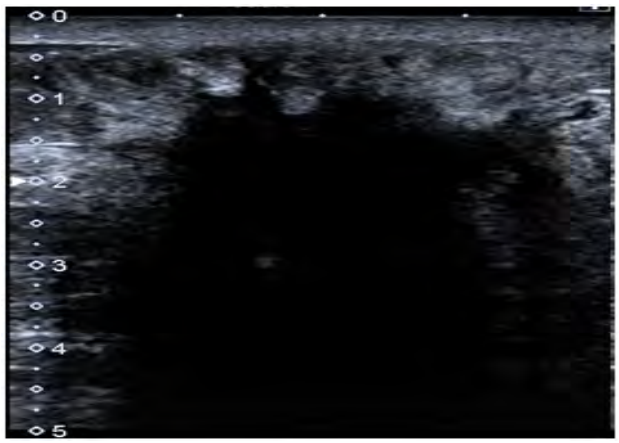

Figure 3: Pregnancy-associated breast cancer in a 38year old lactating woman, 10 months postpartum presented with a palpable mass in her right breast for the prior 2 months. Ultrasonography showed a hypoechoic mass at 10 0' clock position in right breast having irregular infiltrative margins and dense posterior acoustic shadowing. Core needle biopsy revealed invasive ductal carcinoma.

Discussion

Palpable breast mass during pregnancy which resides for more than two weeks should be investigated.[7] Radio-dense nature of breast tissue during pregnancy or lactation, results in decreased sensitivity of standard diagnostic techniques i.e., mammography. Ultrasound is non-invasive diagnostic technique which was initially used to determine the cystic nature of mass. Its use in detection of breast lesions has increased in recent years. The absence of ionized rays in ultrasound makes it low risk for pregnant and lactating women.[8]

Breast ultrasound is the first-line imaging technique and excellent modality in PABC. It has the highest sensitivity during pregnancy and lactation. 9If a palpable mass in breast is observed, sensitivity of USG is 100% and specificity is 86% in such cases.[9-11] We have designed our present study to observe the diagnostic accuracy of ultrasound in the detection of PABC. We included 200 pregnant or lactating with symptomatic breast. Mean age of patient population in our study was 34 ± 11.36 years. Average age reported in literature is between 32 to 38 years which is similar to our population.[4, 12-13]

We have observed PABC in 23% of our subjects and obesity was predominant in our patient population i.e.,110 (55%). Kim et al. conducted a study about clinic pathological features of PABC and also observed that PABC patients were more likely to be overweight (≥ 23.0 kg/m2).[14] Specificity of ultrasound in our study was 98.05%, with NPV, PPV and diagnostic accuracy of 95.56, 92.85 and 95.0% respectively. These values are concordant with literature.[4, 12-14] Sensitivity of the ultrasound in our study is 84.78% for diagnosing PABC. Wang et al have studied the clinic pathological features and diagnosis of PABC. They have found the sensitivity of ultrasound as 86.0%.[15] Sensitivity of our study is consistent with their study and similar studies who report that PABC usually shows a falsely reassuring pattern on ultrasound. However, the ultrasound is preferred over mammography in PABC. Due to high breast density in PABC mammography is not suitable technique.[16-18]

We have observed that diagnostic accuracy of ultrasound is not affected by age, parity, tumor size or obesity. It has shown high sensitivity and specificity of younger to middle aged women. Similarly, in obese or non-obese women the diagnostic accuracy of the modality remained appreciably high. Similar pattern was observed with parity and tumor size.

Our study has a limitation that being a single institution study we could recruit only those patients who were referred to our hospital. Generalization to a larger set of population could not be achieved.

Conclusion

Our study concludes that the ultrasound has high sensitivity, specificity, PPV, NPV and diagnostic accuracy in detection of PABC. It had sensitivity of 84.78%, specificity 98.05%, positive predictive value 92.85%, negative predictive value 95.56% and diagnostic accuracy 95%. The high sensitivity and specificity along with easy availability, low cost, noninvasive and radiation free nature makes ultrasonography a very useful technique for detection of PABC. Moreover, it retains its high diagnostic accuracy with respect to age, parity, obesity and tumor size.

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ORIGINAL ARTICLE

Critical thinking dispositions of baccalaureate nursing students and their educators: A cross-sectional analytical study

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A B S T R A C T

Background: Critical thinking is an imperative outcome of nursing education. However, several factors contribute to the development of critical being including critical thinking dispositions (CTDs).

Objective: This study aimed to assess the critical thinking dispositions and factors affecting critical thinking dispositions of BScN students and their educators in twin city Rawalpindi and Islamabad, Pakistan.

Methodology: A cross- sectional analytical design was used in this study. A consecutive sample of 215 BScN students and 63 educators participated in the study. Data were collected via Pakistan-Critical Thinking Dispositions Scale (P-CTDS) comprising 54 items under the seven constructs; responses were measured on 5-points Likert scale. Data were analyzed with SPSS version 22.

Results: The findings showed that 52% of the educators were at the developed level of CTDs and nearly 48% at the developing level; whereas 76% students were inclined towards CTD and only 23% were found at the developed level of CTDs. Although with considerable difference in the scores of the 7 constructs, both, students and educators obtained highest scores on inquisitiveness and contextual perspective. Similarly, students and educators obtained low score on open-mindedness. The difference between students and their teachers was statistically significant for the total scores of CTDs as well as for the scores of six of seven constructs.

Conclusion: Although educators exhibited stronger CTDs than their students, both have room for improvement, specifically their open mindedness. If educators are willing to challenge their personal assumptions, students will also emulate them.

Keywords: *Critical thinking, critical thinking disposition, nurse educators, BScN students.*

Introduction

With the increasing burden of diseases, rapid advancement in technology and confronting diverse situations requiring optimal decisions in health care delivery, nurses' must possess critical thinking.[1,2] Therefore, critical thinking (CT) is one of the expected out-come of the nursing programs, particularly the nursing degree programs.[2-5] CT is composite of critical thinking dispositions (CTDs) and CT skills. CTDs contain personal characteristics such as truth seeking/intellectual-integrity, perseverance, self-confidence, open-mindedness and inquisitiveness that stimulate CT.[6] CTDs are also known as habits of mind or critical thinking attitude. Whereas, CT skills refer to cognitive skills including information seeking, interpretation, analysis, inference, evaluation and reasoning.[7]

The development of critical thinking skill is interlinked with critical thinking dispositions. However, literature illustrate that it is not necessary that a person having CT skills, use those skills unless he/she is disposed towards CT or internally motivated to think critically.[8] Current literature emphasized that educators' own attitude to think critically is crucial as they are primarily responsible to

develop CT attitude among their students.[9,10] The evidence further supports that individuals who have developed the habit to think critically are more likely to apply CT in their practice.[8] Considering the importance of CT for nurses, nurse educators must possess and nurture critical thinking attitude in their students through role modeling and active teaching strategies that are known to enhance CT.[10,11]

Given the role of CTDs in critical thinking, extensive research has been done worldwide on the phenomenon under the study. Although very limited studies have been conducted regarding critical thinking in Pakistan, none of the study has been found on critical thinking dispositions of nursing students and their educators. Therefore, the current study was designed to investigate and describe the critical thinking dispositions of baccalaureate nursing students and their educators.

The study specifically answered the following questions:

1. What are the critical thinking disposition level of BScN students and their educators?
2. Is there any difference between BScN students and their educators' critical thinking disposition level?
3. Is there any association between educator's demographic characteristics and their critical thinking disposition level?

Methodology

A cross-sectional analytical study design was used to answer the study questions. The population of this study was final year BScN students and their educators from the twin city Rawalpindi and Islamabad. The sample for this study was recruited from six nursing colleges in 3 sectors (public, private, and army), offering BScN program all were recognized by Pakistan Nursing Council. Keeping in mind the available study population that consisted of 236 baccalaureate students in their final semester and 81 nurse educators, a consecutive sampling technique was used to recruit the study participants.[12]

Inclusion criteria for educators required to be full time employee with at-least one year teaching experience. Educators in administrative role and not involved in teaching, were excluded from the study. Alternatively, all nursing students in their final semester of the BScN program in Rawalpindi and Islamabad were recruited. Ethical approval was sought from Institutional Review Board prior to data collection.

Critical Thinking Disposition Scale was used to collect the data.[13] The scale comprised of 54 items that are stated bilingually in English and Urdu, under the seven constructs. Responses of the items were measured on a Likert-scale of 1-5, with one being "strongly disagree" and 5"strongly agree". Thus, the minimum obtained score could be 54, while maximum obtained score could be 270 on this scale. Of the 270, a score less than 50% is categorized as underdeveloped disposition, a score of 50-79% is considered developing disposition, and a score of >80% is viewed as developed disposition. Negative statements were reverse coded. The average time to complete the data collection tool was 15 minutes. The reported content validity of this tool is 0.93.

The tool was pilot tested on 64 BScN interns and no changes were made. Participant of the pilot study are not included in the current study. In this study, the Cronbach's alpha for the Pakistan-Critical Thinking Disposition Scale (P-CTDS) was 0.85. Demographic variables were also added to the scale. Educators were also asked whether they had attended any course or training to enhance their CT. Data was analyzed using Statistical Package of Social Sciences (SPSS) version 22.

Results

Of all the potential participants, 215 students and 63 educators participated in the study, thus the response rate was 91% for students and 78% for educators. As shown in Table 1 and 2, the majority of the study participant whether students or educators were female. Of the 63 educators nearly half of them (50.8%) had only an undergraduate degree in nursing. With regards to the CT preparation of educators' (n=35) attended <12 hours on-job training/workshop, whereas only one participant had 3 credit hours structured course to develop critical thinking.

As shown in table 3, the majority (76%) of the students were found to have developing level of CTD; whereas 23% were at the developed level of CTD. Unlike the students 52% of the educators were found to have developed level of CTD and rest of them in the developing state of CTD.

Table 1: Demographic Characteristics of the Students (n=215)

Variables	Mean ± SD
Age (in years):	
Pre-Licensure BScN	24.06 ± 2.15
Post RN BScN	32.45 ± 5.74
Gender:	N (%)
Male	27 (12.6)
Female	188 (87.4)

Table 2: Demographic Characteristics of Educators (n=63)

Variables	Mean ±SD
Age (in years)	36.64 ± 7.02
Work experience (Years):	12.55 ± 4.92
Teaching	5.74 ± 3.97
Clinical	6.81 ± 5.87
Gender:	N (%)
Female	42 (66.7)
Male	21 (33.3)
Professional Qualification:	
Graduate	30 (47.6)
Undergraduate	32 (50.8)
General Nursing Diploma	1 (1.6)

With regards to the sub-scales of CTD, the majority of the students (78%) scored at the developed level of inquisitiveness. Likewise, about 63% of the students attained developed level score on sub-scale of contextual perspective. A considerable percentage of the students (42-45%) also scored at the developed level on the sub-scales of creativity and truth-seeking. On the subscale of reflection and perseverance, the majority of the students were found to be at the developing level. Likewise, a very low number of students (6.5%) scored at the developed level on the sub-scale of open-mindedness. In general, less than 2% of the students were found at the underdeveloped level of any sub-scales of P-CTDS.

Similar to the students, educators also showed better scoring on the sub-scales of inquisitiveness and contextual perspective compared with the other sub-scales of P-CTDS. As nearly 86-89% of them were found at the developed level of contextual perspective and inquisitiveness respectively. Unlike the students, a significant percentage of the educators (52- 65%) were also found at the developed level, on three sub-scales that are: creativity, perseverance, and truth seeking. However, on the sub-scales of reflection and open-mindedness, a higher percentage of educators (58.7 and 77.8) were found at the developing level, whereas only one educator was found at the underdeveloped level in the sub-scale of open-mindedness.

With regard to the differences in CT disposition between students and educators, the Mann-Whitney test showed a significant difference in their overall CT disposition scores ($p<0.001$). Likewise, on all the sub-scales except creativity, the differences between students' and educators' scores were statistically significant. Although, overall scores showed difference for nurse educators and students, there was consistency among them on the sub-scales of P-CTDS. As on contextual perspective 88.9% of the educators and 62.8% of the students attained developed level of CTDs. While on the sub-scale of inquisitiveness 85.7% of the educators and 77.7% of the students scored at the developed level of CTDs. whereas, educators and students both exhibited low score on sub-scale of open-mindedness (Table 3).

In terms of association between educators' demographic characteristics and their CT dispositions, the Pearson Chi-square analysis showed that gender had significant association with the CT disposition level, as the majority of the female educators attained developed CT disposition level. Likewise, the Kruskal Wallis test showed a significant association of age with CT disposition level. However, no association was found between work experience and CT disposition level.

Table 3: CT Disposition levels of the students (n=215) and educators (n=63)

Constructs	Level of CTDs						Difference b/w students & educators
	Underdeveloped N (%)		Developing N (%)		Developed N (%)		p value
	Students	Educators	Students	Educators	Students	Educators	
Inquisitiveness	1 (0.5)	-	47 (21.9)	9 (14.3)	167 (77.7)	54 (85.7)	0.003
Contextual Perspective	2 (0.9)	-	78 (36.3)	7 (11.1)	135 (62.8)	56 (88.9)	<0.001
Intellectual Integrity /Truth-seeking	1 (0.5)	-	118 (54.9)	22 (34.9)	96 (44.7)	41 (65.1)	<0.001
Creativity	1 (0.5)	-	124 (57.7)	30 (47.6)	90 (41.9)	33 (52.4)	0.10
Perseverance	3 (1.4)	-	133 (61.9)	29 (46)	79 (36.7)	34 (54)	0.04
Reflection	4 (1.9)	-	158 (73.5)	37 (58.7)	53 (24.7)	26 (41.3)	0.03
Open-mindedness	-	1 (1.6)	201 (93.5)	49 (77.8)	14 (6.5)	13 (20.6)	<0.001
Overall	1 (0.5)	-	164 (76.3)	30 (47.6)	50 (23.3)	33 (52.4)	<0.001

Discussion

This study described the level of CT disposition among BScN students and their educators in the twin city of Rawalpindi and Islamabad. The findings showed that compared to the students, the educators possess stronger CT disposition as nearly more than half of them were found at the developed level of CTDs. Whereas, the rest of them were inclined towards CT disposition as they were found at the developing level of CTDs. On the contrary, the majority of students were inclined towards CT disposition, but 23% of them were found at the developed level of CTDs. Using the same Scale, Yasin (2018) reported similar findings about BScN students in Lahore; however, in her sample, about 18% of the students scored at the developed level of CTDs while the majority of them were inclined towards CTDs. These finding implies that both, educators and students could enhance their CT dispositions, concurrent so as with previous studies[1,9,14] In researchers' point of view this may be due to lack of educators' preparedness to apply effective teaching/learning strategies to inculcate CT among their students that warrants further research. Previous studies reported, if more educators possess strong level of CTDs, they will be able to better demonstrate their CT behaviors and influence their students.[10, 11-15] There were other studies that have also reported lower scores on CTDs of the students.[2, 5] However, the findings of present study is comparable only with three constructs; inquisitiveness, open-mindedness and truth seeking of California Critical Thinking Disposition Inventory (CCTDI).[8]

The highest percentage of students showing developed level of CTDs in sub-scale of inquisitiveness indicated the students' high interest and desire for new learning. In the existing literature about CTDs most studies reported similar finding on the sub-scale of inquisitiveness.[1, 5, 14, 16] In researchers' opinion the findings of present study as of student's high response for inquisitiveness may be due to students' frequent exposure to advancement in information and technology and frequent usage of social media. However, in contrast the findings of present study contradicted some previous studies that reported low scores on sub-scale of inquisitiveness.[2, 3]

The second highest response in the present study was noted on sub-scale of contextual perspective that indicated developed level of CTDs and finding are consistent with one of the recent local study. Here its'

important to high- light, both local studies established that first and second highest response on sub-scale of inquisitiveness and contextual perspective respectively indicated students' strong tendency towards developed level of CTDs. On contrarily, very few of the students scored developed level of CTDs on sub-scale of open-mindedness that corresponded with other studies too.[2, 10, 14-16]

Such finding signifies that the students may be intolerant to accept the divergent views if they are not taught in a manner that emphasizes the importance of diversity and divergent views, also ego-centering approach which is deterrence in CT.[5] As literature supported that nursing educational programs are not producing nurses who are critical thinkers. Lack of open-mindedness among students must be addressed by the educational institutions on priority basis, otherwise it may affect the quality of nursing care delivered by graduating nurses.[1, 2, 17]

Overall, more than half of the educators scored developed level of CTDs. These results were consistent with a previous study that may be due to conducive learning environment.[10] With regard to sub-scales majority of the educators attained developed level of CTDs on contextual perspective as highest response. Likewise, their score on the sub-scale of inquisitiveness was also second top response as a large number of participants attained developed level of CTDs. Previous studies on educators also reported similar results on sub-scale of inquisitiveness. Educator's third highest response was in sub-scale of intellectual-integrity/truth-seeking in developed level of CTDs that was also consistent with other studies.[11, 18]

Educators' low score in developed level of CTDs on the sub-scale of open-mindedness was consistent with the studies conducted in Nigeria and South Korea that indicated cultural impact on the study this may inhibit the student's centered approach in teaching.[10,19] On all the sub-scales except creativity significant difference was noted between students' and their educators' level of CTDs. The present study showed similar results as of previous study conducted in Nigeria on BScN student and their faculty members that showed high scores of educators in sub-scales of truth-seeking, open-mindedness and inquisitiveness in comparison with students.[5, 10, 20, 21] The non- significant results of current study in creativity may be due to teacher's lack of ability or interest in creativeness. The lack of creativeness/innovativeness among educators may affect the class room environment as of teacher centered instead student centered being not able to apply advanced teaching learning strategies.[10, 22]

Mann-Whitney test on nonparametric data showed that there was no statistically significant difference found except reflection in overall level of CTDs between the both groups pre-licensure BScN and post RN BScN students. The significant result in sub-scale of reflection may be due to maturity level and work exposure of the post RN BScN students. The Pearson Chi-square analysis of the current study showed that gender and age of the educators had significant association with their level of CTDs. A previous study on pre-service teachers also found association of gender with level of CTDs.[23] In contrast, some of the studies found no association of age with educators' level of CTDs.[9, 17, 24, 25]

Conclusion

Despite the fact that the majority of the students scored developing level of CTDs indicating deficient in developed CTDs, it is encouraging that only one student scored underdeveloped level of CTDs. These findings are satisfying in matter of fact that with a few more efforts by the educators and the Nursing Colleges, students CT disposition may be enhanced further towards developed level of CTDs while building on developing level of CTDs rather starting from underdeveloped level of CTDs. Despite the fact educator possessed developed level of CTDs, even then there is need for improvement. Students who developed the dispositions: contextual perspective, perseverance, reflection, intellectual- integrity, creativity, open-mindedness, and inquisitiveness are more likely to exercise CT in their profession.

The study results emphasized the need that educators should by dynamic and role models in promoting CT among their students. Moreover, teaching institutions should provide enabling environment to the educators through integrated curriculum and infra- structure with educational innovations for application of CT.

Implications of the Study:

Nursing Education

1. Nursing degree programs must include component of CT in curriculum, designing courses, teaching plans and teaching strategies.
2. Students should be given ample time for co-curricular activities so they learn CT through socialization.

Educators

Educators must play their dynamic role to:

1. Become role models in CTDs for students and take charge of their own professional development.
2. Create an environment and demonstrate CT during content delivery: thinking loudly and allowing students to do so.
3. Motivating students to use CTDs for problem solving and decision making in personal as well as professional life.
4. Empower students to ask questions, express their opinions, and learn from mistakes in the safe learning environment.

Nursing Students

Nursing student must show commitment towards their own learning to:

1. Develop habits of questioning and open mindedness to make CT a routine.
2. Change "I do not know" with "I will find out" which exhibits the ability to find out solutions.
3. Practice peer interaction that involves CTDs, collective thinking process for the purpose of meaningful encounters and interpersonal skills.

Administration

Nursing administrators must play an active role in structuring faculty development program to enhance their capacity building and CT on regular basis to develop competent educators as a role models that enable students to mimic CT.

Nursing Research

The study should be replicated on larger samples from various geographical locations with diverse demographic variables in Pakistan for the purpose of generalization. Further studies should focus on following questions that arose from data analysis:

- What are the perception of educators regarding students learning styles and approaches?
- What are the facilitator and barriers in nursing education to develop critical thinking among students?
- What are the educator's perception regarding being prepared to inculcate CT among their students?

Limitations of the Study

The findings of this study may be generalized only in Rawalpindi and Islamabad not on country level as Yasin, (2018) reported much lower number of students who scored developed level of CTDs than the present study. Moreover, participant's mood, attitude, and personal biases at the time of data collection may have affected self- reported responses. In addition, question related to recall e.g., educator's responses regarding their training for critical thinking may have affected the findings of the study.

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ORIGINAL ARTICLE

Effect of formal training workshop on teachers' quality of written feedback in higher education

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[1] Conceptualization of the study and intervention
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[4] Participation in delivery of intervention
[5] Proposal development and participation in delivery of intervention
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A B S T R A C T

Introduction: The significance of written feedback in students' learning is well established in the literature; however, it is contingent on several factors, particularly the quality of written feedback. Many teachers are not formally trained to give feedback that could affect the student learning.

Objective: This study was designed to investigate whether teachers modify their written feedback in response to a formal training workshop on written feedback.

Methodology: Using a quasi-experimental design with pre and post within subject design, 94 teachers participated in this study. As a pre-test, participants were made to provide written feedback on a sample script at the beginning of the workshop. This was followed by a two-day interventional workshop that included discussions and hands on exercises on multiple aspects of written feedback. At the end of the workshop, the participants were again asked to provide feedback on the same script.

Results: Comparisons between the pre- and post-intervention data revealed several differences. The quantity of feedback increased subsequent to the intervention. Reflective questions and suggestions increased as well while appraising, critical, vague, and teachers' own contemplative comments decreased. A rise in feedback on form and writing style was observed after the workshop, as opposed to a slight drop in feedback on content, leading to a more balanced focus. Preceding the workshop, participants gave feedback using symbols such as underlines, tick marks and cross-outs, but after the workshop they were observed to use more phrases or complete sentences. Although some of the desired differences, such as avoiding vague comments and criticism, were statistically insignificant, most of the other, differences in the pre-test and post-test were statistically significant.

Conclusion: This study affirms that a formal training workshop could improve the quality of teachers' written feedback.

Keywords: *Intervention workshop, written feedback, faculty development*

Introduction

Written feedback (WFB) has received tremendous attention from researchers in higher education in recent decades. The increasing demand from university students to submit written assignments requires a comprehensive understanding of the process of feedback on their writing.[1,2] Several researchers have pointed out the value of WFB,[3–8] as an important teaching-learning tool that makes learners aware of their strengths and weakness, enabling them to modify their subsequent performance.[6,7] However, it is quite challenging for the teachers to identify the most effective written corrective feedback[1,9,10] to enhance students' learning.

Dekker et al.[3] has identified that positive questions aligned with the particular student's reflective level triggered more reflection than negative statements. Additionally, the format of WFB was found to have the most significant reflective effect, whereas tone and focus were observed to have moderate and no effect, respectively.[4] Additionally, a disproportion between praise, criticism, correction and suggestions in teachers' feedback is also reported in earlier studies. A study conducted in a private university in Pakistan identified several factors that determine the students' level of acceptance of the feedback.[5] It was observed that teachers fail to strike a balance among praise, criticism and suggestions while giving WFB, which can be discouraging for students. When WFB is centered only on the accuracy[11] of assigned work or correcting errors[12] rather than suggesting ways to improve the work, the opportunity for students' learning is lost.

The feedback often targets the content and fewer comments are given on the style and language.[13] Resultantly, the focus of teachers' feedback directs the students' perception of what aspects are important in academic writing[14] and influences students' response.[15] Providing suggestions to enhance assignment quality promote students' learning as compared to rectifying the errors the made. Another aspect of WFB that affects students' response is the way it has been expressed. While symbols and punctuation marks can be rather cryptic for students, sentences render the feedback clearer. In an analysis of teachers' WFB on 174 student essays, Lee found only 8.6% complete sentences from a total pool of 5353 feedback units. Of these units, 91.4% of the feedback was expressed in the form of symbols such as encircling or underlining.[15]

Numerous studies [3,5,6,16–18] have isolated significant qualities of WFB that affect students' uptake, understanding and utilization of the feedback. Where studies have reported great variations in teachers' practices of providing WFB [5,11,12,14]; there is an emphasis on the provision of context-specific feedback.[1,19,20] Thus, earlier studies have considered teachers' training as instrumental to provide effective feedback.[3,5,21–23] Training can enable the teachers to determine the most effective method of providing feedback in their own teaching context.[1] Nonetheless, hardly a handful of studies, have attempted to examine the effects of teacher training in any aspect of WFB to date.

Ferris [22] trained graduate students of TESOL (Teaching English to Speakers of Other Languages) on how to provide effective feedback to their future students on their written assignments. The study emphasized on providing encouragement and personalized comments. This multi-phasic training required trainees to provide feedback to at least one of their existing students in three ways, verbal, written and electronic. Ferris further emphasizes the need to train and encourage students to utilize the feedback given.[21] This study concluded that quality of feedback is pivotal to reliable assessment and reminded trainees to constantly evaluate their own feedback and its effectiveness.

Salerno et al.[23] reported that brief faculty development workshops were found effective in improving the quality and quantity of feedback provided to students. Their analysis of feedback by faculty members before and after a three-and-a-half-day workshop showed an average of 2.8 to 3.6 comments in the post workshop assessment. Categorization of the comments demonstrated that specific, formative and student-skills-focused comments were provided more often after the workshop.

Even though research [23] bolsters the present study because it also centers on improvement of feedback provided by teaching staff, it is different from the study at hand in two significant ways. First of all, Salerno and colleagues[23] analyzed both verbal and written feedback provided by teachers, even though their focus was on written feedback, while our study is based solely on the latter. Second, the participants in their study gave written feedback on students' performance during encounters with outpatients. Whereas, in this study WFB included teacher's response to students' writing using symbols, codes, comments or overwriting, that aim to guide students.

The present paper describes the effect of interventional workshop, which was part of the second phase of a large-scale research on written feedback. In the first phase of the study, data were collected about teachers' perceptions and practices of WFB [24] and students' perceptions and utilization of WFB. The aim of the second phase of the study was to examine the effect

of a formal training workshop on teacher's performance in providing WFB in higher education institutes in Karachi. Specifically, this study was undertaken to answer the following questions:

1. Is there any effect of a formal training workshop on the quantity of teachers' feedback comments?
2. Is there any effect of a formal training workshop on the expression, tone and focus of teachers' feedback?

For the purposes of this paper, quantity refers to the number of feedback units, including symbols, words, clauses, etc. Likewise, expression means whether the feedback was given in the form of a symbol such as a tick mark or a single word, OR a phrase or sentence. Tone means whether the feedback was framed as praise, criticism, suggestion [25] or reflective question. Focus refers to whether the feedback unit targeted form, content or writing style.[26]

Methodology

Design and Sampling

A quasi experimental design with pre and post-test within subjects [27] was used to measure the outcome of a formal training workshop on teachers' performance for providing written feedback. Considering that teachers' self-development requires interest and commitment, a non-probability sample of teachers was employed from the four disciplines that were represented on a Research group with a goal to improve the practices of Written Feedback in Higher Education. The disciplines included medicine, nursing, education and applied linguistic.

Sample Size and Recruitment of Participants

The total population (N) of teachers across four disciplines was estimated to be 1165. Using the formula of n= Npq / (N-1)D + pq with a bound on error of 0.1, N of 1165 and p of success 0.36 (based on findings [28]) and attrition of 10%, a sample size of 100 teachers was desired for the intervention phase of the study. Heads of the institutions who participated in the first phase of the study were approached and were requested to nominate teachers from their respective institutions. Simultaneously, teachers who had indicated interest for participation in workshop during the survey were contacted via their contact numbers, if provided. They were encouraged to indicate their interest to their institutional head and request for nomination through institution, without declaring their participation in phase I of the study. Not all the teachers who had demonstrated willingness to take part in the workshop accepted the invitation. Thus, other teachers who had not participated in the first stage of the study, were also invited. As shown in table-1, 143 potential participants registered for the workshop, only 99 came to attend the workshop. Of that, 5 teachers couldn't attend the 2nd day of the workshop due to unforeseen circumstances. However, 94 teachers completed the two-day program and took the post test.

Table 1: Number of participants in each workshop

Workshop	Registered participants	Participants who completed two-day workshop
1	27	19
2	28	16
3	28	20
4	40	22
5	20	17
Total	143	94

Description of the Intervention

The intervention consisted of a two–day workshop that aimed to enhance the participants' competence in providing effective WFB. The contents of the workshop included functions of feedback and its link to assessment and students' learning; characteristics of effective feedback including balanced annotation; use of hedges in writing feedback; factors affecting the utilization of feedback; and the development of tools such as rubrics for effective assessment of student work. The contents of the workshop were selected on the basis of a thorough review of the literature on WFB. This content was then contextualized for the teachers' needs as observed in the findings of the first phase of the aforementioned large-scale study on written feedback. The workshop was led by the members of research team, who are faculty members of professorial ranks working in different disciplines of the university. A variety of methods including group reading, presentations, role-plays, intense discussions, and interactive exercises were used to

educate the participants about feedback in the 16 hours' workshop spanning over 2 days,

The workshop was conducted five times and attended by a separate group of participants each time. On the first day, each individual participant was provided with a folder that contained an informed letter of consent, a form enquiring participants' demographic information, the itinerary of the workshop, and a summary of the learning contents of the workshop in the form of general guidelines on WFB. After obtaining their consent, each participant was asked to give written feedback on a sample script of 805 words. The script, taken from an undergraduate student, was on a general topic of – child abuse, so as to avoid being discipline-specific. Folder of workshop was given to the participants after the pre-test was completed. At the end of the intervention, the participants were given another copy of the same sample script which they had corrected on the first day; and were once again asked to provide feedback on it.

Data Organization and Analysis

All the feedback comments were first typed and numbered to save. Next, the quality of the feedback was assessed using a structured tool[13]. This enabled the researchers to code the frequency of various elements of the feedback comments in terms of expression, tone and focus. When a single feedback unit comprised of both symbol(s) and text, it was the text which was used to categorize that particular entry. To ensure consistency in interpretation of the data, it was analyzed by a single researcher (AT), and the principal investigator of the study was consulted for clarification whenever required.

Tone of the comments was interpreted under categories of praise, criticism, suggestion or reflective questions. Praise included comments that highlighted a positive aspect of the student's writing, for example, 'Description of the issue was well-stated.' Criticism referred to comments that highlighted a negative aspect of the student's writing such as 'Minimal and irrelevant literature support.' Suggestions consisted of comments/punctuation that proposed a change in the student's writing, for instance, 'If you remove some points from here you will have more space in the analysis' or made the required correction e.g. 'Most of the people think that the time of childhood is the happiest time in one's life'. Reflective questions were those that prompted learners to think more carefully about what they have written such as 'Do you think society can play any part to combat this issue?'

This data was then entered into SPSS for analysis. Descriptive statistics were applied on the demographic information of the participants and the various aspects of the feedback including the number, expression, tone, and focus of comments. Since the data did not fulfil the assumptions of normal distribution, Wilcoxon sign rank test was used to test the differences between the expression, tone and focus of the comments before and after intervention.

Ethical Considerations

The study was approved by the Institutional Review Committee (2032-SON-ERC-11). Research ethics were strongly abided by in the execution of this study. The participants were free to refuse the invitation to attend the workshop or to drop out at any time. They were asked to sign letters of informed consent to ensure their autonomy, and the comfort of the participants was our utmost concern. Participants' pre-test and post-test papers were marked with ID to ensure their complete anonymity and confidentiality as well as that of their institutes. For the same reason the data analysis files were protected with passwords.

Results

This section briefly describes the demographic details of the participants before presenting an analysis of the results. Results described here include changes noted between pre- and post-intervention, regarding quantity, expression, tone and focus of teachers' feedback comments.

Participants' characteristics

As shown in table 2, of the 94 participants, most were females, had Master's qualifications and were working as senior instructors. A majority of them hailed from the private sector and from the nursing discipline. Ninety percent were teaching in graduate and undergraduate programs. Their responses about their background knowledge of WFB are shown in table 3.

Table 2: Demographic and professional information about the participants

Construct	Categories	N (%)
Gender	Female	73 (78%)
	Male	21 (22%)
Qualification	Bachelors	37 (39%)
	Masters	49 (52%)
	Post-Basic Diploma	8 (9%)
Designation	Instructor	25 (27%)
	Senior instructor	38 (40%)
	Assistant Professor	8 (9%)
	Associate Professor	4 (4%)
	Others	19 (20%)
Discipline	Nursing	72 (77%)
	Education	13 (14%)
	Linguistics	7 (7%)
	Medicine	1 (1%)
	Linguistics	1 (1%)

Table 3: Prior learning about WFB

Method of learning	N (%)
Trial and error	48 (51.1%)
Formal course	20 (21.3%)
On-the-job training	54 (57.4%)
Peers	35 (37.2%)
Supervisor	36 (38.3%)
Attended workshop	9 (9.6%)

Analysis of pre-intervention and post-intervention feedback

Comparison of the pre- and post-intervention feedback showed that the overall mean of the comments increased significantly from 11.9 to 16.3. The number of feedback units given by a single teacher ranged from 0 to 40 in the pre-test and 0 to 60 in the post-test. Although the overall quantity increased, it is noteworthy that similar to the pre-test, 2% of the participants provided no feedback in the post-test. However; these were not the same participants who provided zero feedback in both pre- and post-test.

Feedback was expressed in either the form of single words or symbols such as tick marks, underlines, question marks, crosses or happy faces, or in the form of sentences or phrases such as 'Well done!'. The use of both expressions in pre- and post-test is shown in Table 4. Results indicate that the use of symbols or single words remained more or less stable while the use of phrases or sentences increased after the workshop. However; the difference was trivial.

Table 4: Expression of written feedback

Unit of expression	Pre-intervention N=94 Mean ± (SD)	Post-intervention N=94 Mean ± (SD)
Symbols or single words	6.16 ± 6.9	6.22 ± 8.25
Sentences or phrases	9.05 ± 6.44	10.07 ± 6.01
Total Units	15.21 ± 10.56	16.30 ± 11.16

During data analysis, two additional categories had to be created that had not been anticipated by the researchers. These had to be formulated due to their occurrence in the WFB. One was teachers' contemplation, which consisted of statements expressing teachers' extempore thought on the students' writing, such as 'Children should share their bad and good experiences with their parents, which can help minimize crime. The second was vague comments, which referred to unclear/ungrammatical statements, for example, 'Psychological abuse explanation' or 'Argument of mentioning of problem would resurrect with corp. and relevant to actual problem.' Some participants even re-wrote extracts from the sample script instead of giving actual feedback. Such comments were also classified as vague. In terms of tone of the feedback, as can be seen in table 5, suggestions and reflective questions significantly increased after the intervention (p-value <0.05) whereas appraising, critical, contemplative and vague comments decreased.

Feedback comments were analyzed as targeting particular aspects of the student's writing in the sample script. One aspect was 'form'; that is, language, grammar and mechanics. A second aspect was 'content', including subject matter, usage of literature, relevance, flow of ideas, completeness, etc. Comments also focused on 'writing style'; for example, word choice, originality, referencing and citation. Table 6 summarizes the

differences in focus of comments between the pre- and post-tests.

Table 5: Tone of the comments

Comment type	Pre-intervention Mean (SD)	Post intervention Mean (SD)	p value
Praise	1.54 (1.96)	1.35 (1.68)	0.468
Criticism	3.91 (4.1)	3.82 (4.95)	0.319
Suggestion	4.86 (6.22)	6.34 (8.24)	0.019*
Reflection	1.04 (2.09)	1.83 (2.47)	0.001*
Teachers' Contemplation	0.5 (1.19)	0.29 (0.70)	0.215
Vague	3.26 (4.45)	2.64 (3.80)	0.018*
Total Comments	11.95 (9.8)	16.3 (11.1)	0.000*

*Level of Significance: 0.05

Table 6: Focus of the comments**

Focus area	Pre-intervention Mean (SD)	Post-intervention Mean (SD)	p value
Form	3.70 (5.4)	4.01 (6.83)	0.870
Content	5.0 (4.1)	4.96 (3.12)	0.987
Writing Style	3.33 (3.83)	4.68 (4.78)	0.001*
Total	12.04 (9.87)	13.66 (11.1)	0.076

*Level of Significance: 0.05

**Excluding vague comments

Focus on form did not deviate much while focus on content decreased slightly. The only statistically significant difference was observed in this dimension of feedback, that is, a considerably greater focus on writing style (p-value <0.05).

Discussion

This study aimed to examine the effect of formal training on teacher's performance in providing WFB through a two-day interventional workshop. Notably, a majority of the sample came from nursing while most of the refusals were from medicine and linguistics. The higher percentage of female teachers in our sample is representative of gender composition in Nursing. One possible reason for the refusal from the field of medicine may have been that in Pakistan, WFB is not generally practiced at both undergraduates and graduate levels in most of the medical schools. And, the good response from nursing could be that WFB is an important component of nursing programs at all levels. Moreover, three out of six members of this research team were nurse educators whose credibility might have attracted more nursing faculty from their networks to attend the workshop. The outcome of the post-test yielded a few anticipated results yet other findings were unexpected.

Quantity of feedback had been one of the topics of discussion in the interventional workshop. Perhaps this is why the total number of feedback units increased from 1419 to 1500 which was expected, albeit not by a significant number. This is in line with findings [23] that feedback comments given by teachers increased from an average of 2.8 to 3.6.

Lee[15] reports that teachers more frequently use symbols instead of complete sentences, while teachers in the present study were observed to use more sentences in both pre- and post-tests. Nonetheless, the frequency of symbols was still high. In the post-test, there was a 2% decline in the use of symbols. One of the topics discussed in the workshop was that single words and symbols were often unclear to students, which is why it was recommended that teachers write phrases or complete sentences. Yet the decrease in the use of symbols was low. Perhaps it takes time to change the practice. This reason for the underuse of sentences is especially plausible because language has already been acknowledged as a limitation for some of our participants. Another reason for the continued prevalence of symbols in WFB could be due to the fact that grading checklists were part of the discussion and participants had been given a sample checklist which contained symbols, so they may have assumed that the symbols given in the sample checklist would be comprehensible to the researchers. In reality, however; the symbols in the provided checklist were meant to be used only after explaining each to the students.

Both pre- and post-test results contrasted with findings that teachers' comments are seldom suggestive. [11,12]

Roughly 35% of participants' comments in both tests of the present study were suggestive. It also came as a surprise that praise decreased in the post-test by nearly 2%. This was despite vigorous discussions in the intervention that the literature on WFB[3] highlights students' demand for a balance between praise and criticism, and that the former serves as an important motivator for learners. Criticism also decreased by 2.5%. It is conjectured that the reduction in praise was correlated with an increase in focus on writing style because there were some serious organizational problems with the paper that teachers might initially have overlooked before they learned in the workshop that content was not the only aspect of students' writing that mattered.

Similarly, on average, less number of vague comments were found in the post-test of a study,[23] but the difference was statistically insignificant in the current research. The nature of most of the vague comments in our sample betrayed teachers' low level of proficiency in English as such comments contained misspelling and mechanical errors, incorrect word choice and tense, as well as awkward sentence structure. Lack of proficiency might in fact have been the main underlying cause of vague feedback. This conjecture is supported in research[29] which suggest that effectiveness of WFB is hindered by teachers' own incompetence in English.

The percentage of reflective questions increased by a statistically significant margin subsequent to the intervention. This was an encouraging finding, because the literature[3,5] shows that reflective questions have the most considerable effect in terms of facilitating students' own reflection on their writing.

Markers' own contemplations on the sample script were puzzling. Such comments, as exemplified in the findings, seemed to serve a cathartic purpose rather than aiming to guide students. Occurrence of such type of WFB has not been highlighted in any previous study. It was encouraging to note that contemplative comments nearly halved following the workshop. This shows, although not inarguably, that the workshop facilitated participants in developing a better understanding of the desired and undesired practices in the provision of WFB, which could improve the quality of their WFB. It is recommended that teachers should keep their contemplations to themselves, so as not to confuse students or waste their time. Usually, students expect that all the comments are for them so if the teacher writes something for her/his own sake it could overwhelm students. If, however, such comments are to be retained, it should clearly be mentioned that they are for the teacher's own use.

With regard to the focus of WFB, it was varied throughout the sample as reported in a previous study.[14] For instance, focus on form stayed nearly the same in both pre- and post-test. On the other hand, focus on content decreased by approximately 4%, which likely happened due to the discussion in the workshop that content was not the only important aspect of students' writing. Participants were seen to provide considerably greater WFB on writing style after the intervention, including comments on word choice, originality and referencing.

On the whole, the present study confirmed findings[23] that interventional workshops can indeed bring about a change in teachers' feedback in terms of quantity, expression, tone and focus. One must bear in mind though that they studied the effects of the workshop for 3 months whereas in our study, only the immediate effects of the intervention were observed. However; both studies show that improving teachers' written feedback practices through a workshop is a plausible strategy.

One major limitation of this study was the lack of a record of feedback practices over a period of time, which could have served as a more credible indicator of change in practice. "In-service workshops designed to improve teaching skills often have only short-term effects and rarely involve teachers in an ongoing process of examining their teaching".[30] In the present study, the differences between the pre- and post-test could have been a result of the Hawthorne effect[31] which is a risk inherent in nearly all intervention studies in which humans are under observation. If post-intervention outcomes are observed in the long term, it is likely to minimize the Hawthorne effect, because human behavior can be modified to please an observer only for a limited period of time.

Although four disciplines were including in the study, most participants came from nursing. Therefore, some

caution should be exercised in generalizing the findings to all four disciplines. In addition, sampling was non-probability, which may also have slightly skewed the results.

Conclusion

In concurrence with Haughney[22] this paper reaffirms the need to train teachers in the provision of helpful feedback. The present paper clearly showed that interventional workshops have the potential to enhance the quality of teachers' WFB. This judgment is especially significant for the health sciences or other similar disciplines, in which teachers are hired on the basis of their expertise in the field without formal training in education. Teachers from such disciplines would need mandatory in-service training, enabling them to reap maximum benefits from WFB. That being said, the eventual goal of research in this field is to discover the optimum means to facilitate teachers in making their WFB practices sufficiently effective and meaningful to enhance student learning and utilization.

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ORIGINAL ARTICLE

Influence of various demographic factors on nutritional status of children under five years of age

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Author`s Contribution

[1] Conceived, designed, statistical analysis & editing of manuscript
[2-3] Data collection and manuscript writing
[4] Statistical analysis and proof reading of the manuscript
[5] Designed the study, review and final approval of manuscript

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A B S T R A C T

Background: Malnutrition in under five children is prevalent in our country. It makes them prone to infections and increases child mortality. This can be controlled by identifying and modifying the predisposing factors.

Objective: To assess nutritional status and to analyze the influence of various demographic factors on nutritional status of under five children.

Methodology: This cross-sectional study was conducted in Shifa Falahi and Community Health center in Islamabad over a period of 2 years (June 2018 till July 2020). Children under five years of age were included. Information was collected from mothers on a self-designed questionnaire. Weight and height of children was recorded and classified according to WHO Z score. Data was evaluated on SPSS 20. Univariate analysis was done to determine independent effect of each predictor on outcome.

Results: Total of 280 patients were enrolled. 162 (57. 9%) of them were malnourished. Stunting was seen in 24.6% cases, while 26.1% were underweight. Wasting was seen in 19.6% cases. More males were stunted (27.9%) and underweight (27.27%) as compared to females (21.2%) and (24.8%) respectively. Low household income (p value 0.014), poor maternal education (p value 0.018), joint family system (0.002), unboiled drinking water (0.008) and repeated diarrheas (0.02) were found significantly associated with malnutrition. Most of the mothers (>75%) had adequate knowledge of breast feeding, vaccination, seeking medical advice for their babies.

Conclusion: All forms of childhood malnutrition are prevalent. Poor socioeconomic status and maternal illiteracy are strong contributors towards malnutrition. Unboiled drinking water and diarrheas are further aggravating the nutritional status of children.

Keywords: *Malnutrition, anthropometry, undernutrition, stunting.*

Introduction

Adequate nutrition, in early childhood, is essential to ensure a strong immune system and proper physical and intellectual development. Childhood malnutrition is generally taken as undernutrition until mentioned the other way round. All over the globe there are 165 million malnourished children under five years of age.[1,2] Malnutrition is the root cause of morbidity and mortality among the children. The risk of death becomes nine times higher for a child suffering from malnutrition as compared to a healthy subject.[2] For the survivors, it compromises their physical and mental development, which results in poor health condition and academic achievement. It has

been estimated that 170 million (30%) of children under the age of five in the world are moderately or severely stunted, and 110 million (19%) are moderately or severely underweight.[3]

This burden of malnutrition is not evenly distributed in different regions of the world. More than half of world's malnourished children live in South East Asia (India, Bangladesh and Pakistan).[4] It is therefore one of the major public health challenges in these countries including ours. Compared to our neighboring countries, Pakistan has one of the highest levels of prevalence of child malnutrition.[5] According to the National Nutrition Survey 2011, 33% of all children were underweight, nearly 44% were stunted, 15% are wasted.[6] In Pakistan, nearly 800,000 children die every year; 35 per cent of them, i.e. 280,000 deaths, occur due to malnutrition.[7] In the last two decades, there has been almost no reduction in the prevalence of child malnutrition in Pakistan compared to our neighboring countries.[6,7]

Multiple factors have been identified contributing towards childhood malnutrition. These include low birth weight, inadequate breast feeding, inappropriate weaning, maternal illiteracy, lack of proper knowledge of nutrition, micronutrient intake, parity, birth spacing, household socioeconomic status, poor sanitation, vaccination, and infectious diseases.[8] Well-nourished children grow naturally and perform to the best of their abilities in academics, they remain healthy both physically and mentally and result in less burden on hospitals and parental worries.

Pakistan demographic and health survey 2017-18 shows stunting of 24.4% in capital city of Islamabad while severe stunting is 6.8%. There is dire need to look at the current situation.[9,10] Pakistan being a developing country is facing double burden of malnutrition and poverty, both interlinked. Reduction in this burden of malnutrition will not only improve health and quality of life of our population but it will also increase economic productivity. Identifying the modifiable factors and working on these factors is the only way out for us. This study emphasizes on the factors affecting malnutrition in children under 5 years of age.

Methodology

This cross-sectional study was conducted in Islamabad Pakistan, in Shifa Falahi and community health center over a period of 2 years i.e., June 2018- July 2020 and comprised children of <5 years of age. Sample size was 280 (as per sample size calculator Rao Soft Confidence interval 91%). Approval was obtained from the institutional review board Shifa International Hospital (IRB #317-166-2013). Informed written consent was taken from mothers. Simple random sampling technique was used. The data was collected on a self-designed and semi-structured questionnaire.

Study indicators that were recorded included, ethnicity, maternal factors like age, education, profession, father related factors like age, education, income, family set up, total family members, source of drinking water and sanitary system. Data regarding child included age, gender, anthropometry (including height, weight mid upper arm circumference) child's birth weight, breast feeding duration, weaning, dietary habits, repeated diarrheas, vitamin supplementation. Mothers' knowledge about diet, hand washing practices, vaccination and doctors' visits was assessed.

The study population's characteristics were summarized using means with standard deviations (SD) for the continuous variables and percentages for the categorical variables. Predictors of childhood malnutrition (stunting, wasting, and under-weight) were investigated using logistic regression analysis. Univariate analysis was conducted to determine independent effect of each predictor on outcomes. Adjusted OR were calculated to study the predictive power of independent study variables in relation to childhood malnutrition. All statistical analyses were performed using SPSS version 20.0 with the statistically significant set at p value≤0.05.

Study definitions

Stunting: Stunting reflects low height for age z scores. The cut off level of -2.0 z score was used for stunting -3.0z for severe stunting.

Wasting: Wasting is based on low weight for height z scores. A cutoff level of 2.0 was considered as wasted child.[11]

Underweight: Underweight is defined as low weight for age z scores. It was based on cutoff value of 2.0 standard deviation z score.[11]

Results

Study population comprised of 280 patients of age less than 5 years.

Sociodemographic characteristics:

Sociodemographic characteristics are shown in table 1. Joint family system was found in 162(57.9%) cases. Families who were living in accommodations with good sunlight exposure were 170(60.7%). Unboiled drinking water was being used by 206(73.6%) families while closed sanitation system was found in 264(94.3%) cases.

Table 1: Sociodemographic characteristics

Indicators		
Gender	Number (n)	Percentage (%)
Male	143	51.1%
Female	137	48.9%
Age in years		
<1 year	57	20.3%
1-2 years	64	22.8%
2-3 years	63	22.5%
3-4 years	34	12.1%
4-5 years	62	22.1%
Mothers' education		
No formal education	79	28.2%
Primary	25	8.9%
Secondary	83	29.4%
Higher	93	33.2%
Fathers' education		
No Formal Education	63	22.5%
Primary	23	8.2%
Secondary	85	30.3%
Higher	109	38.9%
Mothers' profession		
Housewife	240	85.7%
Working	40	14.3%
Household income		
5000	13	4.6%
5000-10000	66	23.6%
>10000	201	71.8%
Family size		
1-5	154	55%
6-10	99	35.3%
>10	27	9.6%

Prevalence of stunting

Stunting was found in 66(24.6%) children. It was seen slightly higher in boys 40 (27.9%) than in girls 29 (21. 2%). Severe stunting was seen in 44(15.7%) children. Similarly, severe stunting was also higher in boys 24 (16.7%) than in girls 20 (14.6%). Stunting was found more in younger age groups while it decreased in 4-5 years' age group as presented in Table 2.

Prevalence of wasting

Wasting was seen in 55(19.6%) of total patients. While 67(23.9%) had severe wasting. Girls 33(24%) had more wasting as compared to boys 22(15. 4%). Wasting was found more in children of 2-4 years age group. On the other hand, 46(16.5%) children were overweight and 7(2.5%) were obese as presented in Table 2

Prevalence of underweight

Overall, 73 (26.1%) children were underweight and 59 (21.1%) were severely underweight. Both boys and girls were equally underweight and all age groups were affected as presented in Table 2.

Large family size (0.00), low birth weight of baby (0.00), junk food daily (0.00), only milk or increased milk consumption (0.001), introduction of meat after 2 years of age (0.002), were found statistically significant with stunting.

Maternal illiteracy, low birth weight and increased milk intake (0.006), low income, unboiled water, poor hand washing practices, daily junk foods intake, large family size were found statistically significant with underweight.

Figures 1 and 2 present the association of stunting and wasting rates by average household income respectively. The prevalence of stunting and wasting was higher in children of poorest households.

Determinants of malnutrition

Certain factors were found associated with stunting, wasting and underweight. Shown in table 3. Unboiled drinking water was found significantly associated with all forms of malnutrition. While low maternal education was found associated with stunting and wasting. Low income, repeated diarrheas, joint family system, sanitary system was associated with stunting.

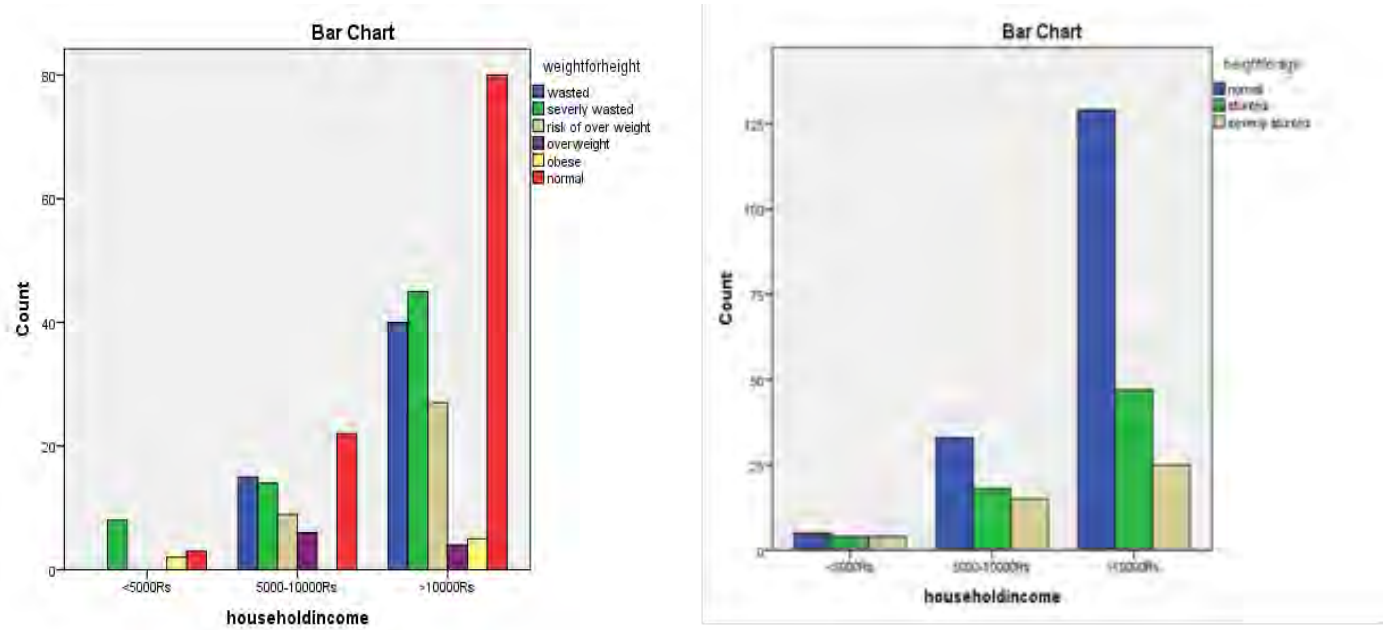

Figure 1 and 2: Association of stunting and wasting rates by average household income respectively.

Table 2: Prevalence of stunting, wasting and underweight under 5 years of age

Total number of children		Stunting		Wasting				Underweight	
		stunted <-2SD	severely stunted <-3SD	wasted <-2SD	severely wasted <-3SD	Overweight	obese	Underweight <-2SD	Severely underweight <-3SD
N		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
280		69 (24.6%)	44 (15.7%)	55 (19.6%)	67 (23.9%)	46 (16.5%)	7 (2.5%)	73 (26.1%)	59 (21.1%)
Gender									
Boys	143	40 (27.9%)	24 (16.7%)	22 (15.4%)	33 (23%)	23 (16%)	6 (4.2%)	39 (27.27%)	30 (20.9%)
Girls	137	29 (21.2%)	20 (14.6%)	33 (24%)	34 (28.4%)	23 (16.7%)	1 (0.7%)	34 (24.8%)	29 (21.1%)
Age groups (In Years)									
<1	57	16 (28%)	18 (31%)	10 (17.5%)	20 (35%)	6 (10.5%)	4 (7%)	18 (31.5%)	17 (29.8%)
1-2	64	15 (23.4%)	14 (21.9%)	9 (14%)	17 (26.5%)	14 (21.8%)	1 (1.5%)	17 (26.5%)	13 (20.3%)
2-3	63	18 (28.5%)	8 (12.6%)	15 (23.8%)	16 (25.3%)	7 (11.11%)	2 (3.1%)	25 (39.6%)	13 (20.6%)
3-4	34	9 (26.4%)	3 (8.8%)	9 (26.4%)	12 (35.2%)	5 (14.7%)	0	6 (17.6%)	13 (38.2%)
4-5	62	11 (17.7%)	1 (1.6%)	12 (19.3%)	2 (3.2%)	14 (22.5%)	0	7 (11.2%)	3 (4.8%)

Table 3: Results of univariate logistic regression analysis showing determinants of malnutrition

Parameter	Stunting		Underweight		Wasting	
	OR (95% CI)	p value	OR (95% CI)	p value	OR (95% CI)	p value
Mothers' education Uneducated educated	 1.39 (1.23-1.56) 1.62 (1.52-1.72)	0.018	 1.35 (1.24-1.47) 1.51 (1.44-1.58)	0.019	 3.8 (3.4-4.3) 3.4 (3.1-3.7)	0.156
Joint family yes no	 1.59 (1.47-1.70) 1.51 (1.38-1.65)	0.002	 1.51 (1.44-1.59) 1.40 (1.31-1.49)	0.065	 3.6 (3.3-3.9) 3.4 (3.0-3.8)	0.338
Drinking water Boiled Unboiled	 1.44 (1.27-1.61) 1.60 (1.49-1.70)	0.008	 1.59 (1.48-1.70) 1.42 (1.35-1.49)	0.013	 3.0 (2.6-3.5) 3.7 (3.4-4.0)	0.012
Repeated diarrheas Yes no	 1.77 (1.57-1.96) 1.50 (1.40-1.60)	0.020	 1.45 (1.32-1.58) 1.47 (1.40-1.54)	0.796	 3.3 (2.8-3.9) 3.6 (3.3-4.8)	0.428
Sanitary system open closed	 1.87 (1.50-2.24) 1.54 (1.45-1.63)	0.011	 1.56 (1.31-1.80) 1.46 (1.40-1.52)	0.454	 3.2 (2.2-4.2) 3.5 (3.3-3.8)	0.511
Low birth weight Yes no	 1.92 (1.51-2.33) 1.54 (1.45-1.63)	0.74	 1.76 (1.49-2.04) 1.45 (1.39-1.51)	0.028	 3.2 (2.1-4.3) 3.5 (3.3-3.8)	0.533
House hold income <5000 5000-10000 >10000	 1.92 (1.51-2.32) 1.72 (1.54-1.90) 1.48 (1.38-1.58)	0.014	 1.61 (1.34-1.88) 1.50 (1.37-1.62) 1.45 (1.38-1.52)	0.457	 3.3 (2.2-4.5) 3.4 (2.9-3.9) 3.6 (3.3-3.9)	0.713

Knowledge and practice of mothers:

Most of mothers (96.4%) 270 have adequate knowledge of hand washing, start of breast feeding (90.4%) 253, weaning (76.4%) 214, vaccination and regular checkups (79.3%) 222 of the child .252 (90%) consult a doctor for illness of child yet 23.2% frequently visit religious peers for seeking advice regarding child's illness.

Discussion

This study is one of the very few local studies using WHO, Z score for classification of childhood malnutrition. The results of our study reinforced that malnutrition is widespread among the children under-five year old, and has not improved since last two decades.[2,10] As per Pakistan's demographic and health survey 2017-18, 38% children are stunted and 17% are severely stunted while we found 24.6% stunted and 15.7% severe stunting.[11] The difference in numbers is probably because our study included children of Islamabad region only.

In the same survey 7% of children were found wasted while 2% had severe wasting which is a number far less than we observed 19.6% and 23.9% respectively. Underweight and severely underweight figures of ours were also high i.e., 26.1 and 21.1% respectively. A sub analysis of PDHS 2013 showed similar high figures of underweight i.e., 26.7%.12 Failure to achieve significant improvement in malnutrition figures is observed. Instability of governments, inflation, lack of policies to facilitate poor and low-income families are contributing towards this condition.

The trends of malnutrition are not the same in South Asian region, with Pakistan and India being the most affected countries having stunting and underweight rates in the range of 40-50% and 30-40% respectively.[12] Our neighboring country shows figure that is even higher than ours. A community based cross sectional survey in our neighboring country India Haryana showed burden of underweight and severe underweight 41.3% and 14% respectively.[13] Countries like Bangladesh and Sri Lanka have achieved significant improvement in child

malnutrition in recent years.[12] Slight male predominance of malnutrition in our study is in contrast to the gender bias observed in certain local studies.[14]

At 6-11 months of age malnutrition was found in greatest frequency by Zulfiqar et al and Achakzai.[14,15] We noticed stunting and underweight children mostly of age 2-3 years while wasting was most frequent at 3-4 years of age. Breast feeding is discontinued by this age and child is totally on weaning diet, at this time. There are many myths involving complimentary feeding of children and pregnant women which acts as a base to the poor health outcomes in children.[16] Cultural norms and average household food probably is the contributing factor for this age malnutrition. If we are more vigilant to supplement the child with multivitamins and counsel for optimal diet, this can improve the condition.

The results of our study also revealed that there was a highly significant chance for being of stunted, wasted and underweight in children belonging to the lower quintiles as compared to highest quintiles, and almost similar findings were reported in studies from Africa.

Low household income is significantly associated with overall malnutrition in our study as was seen by Stavros and Emil.[17-19] Low family income forces people to opt unhealthy food options that promotes malnutrition and infections which cannot be properly addressed by family due to financial issues. A survey of 12 countries proved that an increase in the income of individual households, or of the nation as a whole, reduces malnutrition by the same proportion.[20] Low level of parental education, especially of the mother, is known to be significantly associated with childhood malnutrition as is the case in present study.[13,18,19,21]

There is dire need to improve the educational status of females. It is 46.47% as per 2017 statistics of Pakistan. It has been found that children of educated mothers are more nourished than illiterate mothers. A study from Indonesia shows that a mother's education is a strong predictor of her child's nutritional improvement over time.[22] In Pakistan we have mostly joint family system of living. This has significant association with stunting as reported by Aurengzeb et al in their study of hospitalized children as seen in our study.[18] In Pakistan only 20% population has accessibility to safe drinking water. It is significantly associated with malnutrition.[21] Being simple modifiable factor, this can be addressed at household level. Repeated diarrheas are found to be significantly associated with (0.020) stunting in our study. Prevalence of diarrhea in under five children is 23.1% as per PDHS 2012-13. It can cause mortality in the face of malnutrition as described by Radhini et al.[23]

One of the limitations of our study was that maternal nutritional status could not be assessed as the child was not always accompanied by mother and this was a single encounter data collection. Maternal malnutrition has significant impact on child's nutritional status as described by Attia et al.[24] In addition to reinforcing and counselling for child's diet, mothers should also be counselled for their own diet and supplements on the same visit. Every factor contributing towards malnutrition is interlinked. In spite of having knowledge of all of them, we are unable to control malnutrition in our children. Counselling for awareness of mothers and families and policies at government level to cater these issues is required.

Conclusion

We have high magnitude of childhood malnutrition without any significant improvement for last decade. There is dire need to look into the significant factors of poverty, illiteracy and provision of safe drinking water at government level to deal with this serious issue.

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ORIGINAL ARTICLE

Effects of Surah Al-Rehman on pain, oxygen-saturation, and vital signs in post CABG patients: A Pilot Study

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Author`s Contribution

[1] Conceptualization of study and investigation
[2] Supervisor of the study
[3] Committee member

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A B S T R A C T

Objective: The main objective of the study was to determine the effects of Surah Al-Rehman on post CABG patients' pain level, oxygen saturation, and vital signs.

Methodology: A quasi-experimental pre and post-test design was used with a sample size of 60 patients in two tertiary care Hospitals, from July 2018 to September 2018. A non-probability convenient sampling method was used to recruit the participants. Post CABG adult Muslim patients were the study participants. Surah Al-Rehman's recitation in the voice of the Qari Abdul Basit was the intervention for the current study. At a significance level of p-value ≤ 0.05, a repeated measure ANOVA was applied to determine the effects of Surah Al-Rehman on the outcome variables, which were patient's pain level, oxygen saturation level, and vital signs including heart rate [HR], respiratory rate [RR], systolic and diastolic blood pressure.

Results: Overall, Surah Al Rehman had shown statistically significant effects on the participants' pain level ($p<0.001$), oxygen saturation level ($p=0.01$), respiratory rate ($p<0.001$), and diastole blood pressure (DBP, $p=0.04$). A minimum change in the pre and post values of HR and systolic blood pressure (SBP) was also observed, but statistically, this change was insignificant (HR, $p=0.13$ & SBP, $p=0.47$).

Conclusion: Findings of the current study demonstrated that listening to the recitation of Surah Al-Rehman could decrease pain level, RR, DBP and enhance oxygen-saturation in post CABG patients.

Keywords: *Surah Al-Rehman, CABG, pain, SPO_2, vital signs*

Introduction

Cardiovascular Diseases (CVDs) are one of the major disease burdens worldwide.[1] Coronary Artery Diseases (CAD) are one of the CVDs with five times higher risk factors in south Asian Countries as compared to other countries. Coronary Artery Bypass Grafting [CABG] is the most common treatment of the CAD. Nearly 70% of patients having CAD require CABG.[2] In 2016, approximately 11121 CABGs in Bangladesh and 5500 CABGs were performed in Sri Lanka. Whereas 20,000 CABGs were performed in Pakistan.[7] CABG is a complex and prolonged surgery, which requires patient's post-operative management in Intensive Care Unit (ICU). In the ICU patient has multiple invasive and non-invasive lines such as an endotracheal tube, central line, arterial line, chest drain, and folly's catheter; Leg wound and chest wound incision, all of these factors cause severe pain to the patient.[4]

Post-surgical pain after the CABG procedure is a common factor that affects the recovery of the CABG patients[5]. It is an unpleasant sensory and emotional experience of the individuals due to tissue damage. In the CABG procedure pain occurs due to the incision of the tissue, intra-operative tissue retraction, multiple intravascular cannulations, and a chest tube for drainage after the surgery. Hence, these factors cause severe pain in the chest. Due to the chest pain, the patient cannot take

a deep breath, it causes cough that complicates respiratory distress leading towards decreased oxygen saturation level in the body. The decreased oxygen level could hinder the in wound healing. Moreover, unrelieved postoperative pain can lead to immobilization and may result in complications such as deep vein thrombosis, coronary ischemia, pneumonia, insomnia, and demoralization.[4]

Furthermore, pain contributes to the anxiety level of CABG patients in ICU. Pain culminates into anxiety, which can cause tachycardia, helplessness, and loss of confidence decreasing patient immunity against the disease; thus, adversely affect the patient's recovery.[6] Cardiac surgery pain can be treated with pharmacological and non-pharmacological methods. In pharmacological methods, sedatives and analgesics are extensively used to control physiological stress and pain during and after surgery. These medicines are very costly and may lead to prolonged ventilation and delayed recovery, and consequently an increase in the cost of care.[7] In addition to the pharmacological methods, non-pharmacological methods are encouraged.

Non-pharmacological therapies have become very popular due to no side effects. CABG pain can be relieved through some measures such as muscle relaxation, cold gel pack, massage therapy, music therapy and prayer therapy.[8] Music therapy is a simulator that triggers psychological responses from the listener and thus controls the pain.[9] Music therapy is the best protective and safe therapy to control the pain and physiological stress.[9]Music therapy can have significant effects on vital signs and pain level[10] and thus, it help in controlling blood pressure and respiratory rate.

A comparative study of the Quranic recitation and music sound on the anxiety and vital signs of the patients reveals that music and Quran sound had a positive effect on the vital signs and anxiety level.[11] Likewise, Surah Al-Rehman is also known to be effective in treating depression.[7] Although the effect of Surah Al Rehman on pain is not studied, some researchers have reported that other verses of the Quran including Surah Fatiha and Surah Yaseen can decrease the pain.[12] Since Surah Al Rehman is very significant in terms of its name and it is most Rhythmic Surah; therefore, it could be more effective in managing pain. The purpose of the study is to determine the effects of Surah Al-Rehman on patient's post-operative pain, oxygen saturation level and vital signs in post-CABG patients during their hospitalization in ICU.

This study aimed to answer the following research questions:

1. What is the effect of Surah Al-Rehman on post-operative pain in CABG patients during their recovery in the ICU?

2. What is the effect of Surah Al-Rehman on the post CABG patient's vital signs during their recovery in the ICU?

3. What is the effect of Surah Al-Rehman on the oxygen saturation level in the post-CABG patients during their recovery in ICU?

A detailed conceptual framework (Figure 1) was made which is summarizing that how post-CABG pain along with the activation of the sympathetic nervous system lead to delayed wound healing and how these complications can be overcome with the intervention of Surah Al-Rehman. There are multiple factors such as sternum incision, leg incision; the number of grafts, intensive care environment (machines, noises), fear due to uncertain outcome and multiple invasive monitoring lines and drains, which aggravate pain and anxiety.

Pain and anxiety activate the sympathetic nervous system, as the heart rate increases it leads to arrhythmias and due to arrhythmias coronary blood supply is compromised. Similarly, when respiratory rate increases, the patient hyperventilates, wash out carbon dioxide and end up with respiratory alkalosis. Moreover, blood pressure also increases as a result of pain which can increase coronary pressure, and the risk of graft rupturing. Thus, all these changes in the hemodynamics ultimately lead to hypoxemia with poor wound healing, delayed recovery, and rehabilitation. So, with the use of Surah Al Rehman all these complications can be overcome with better recovery.

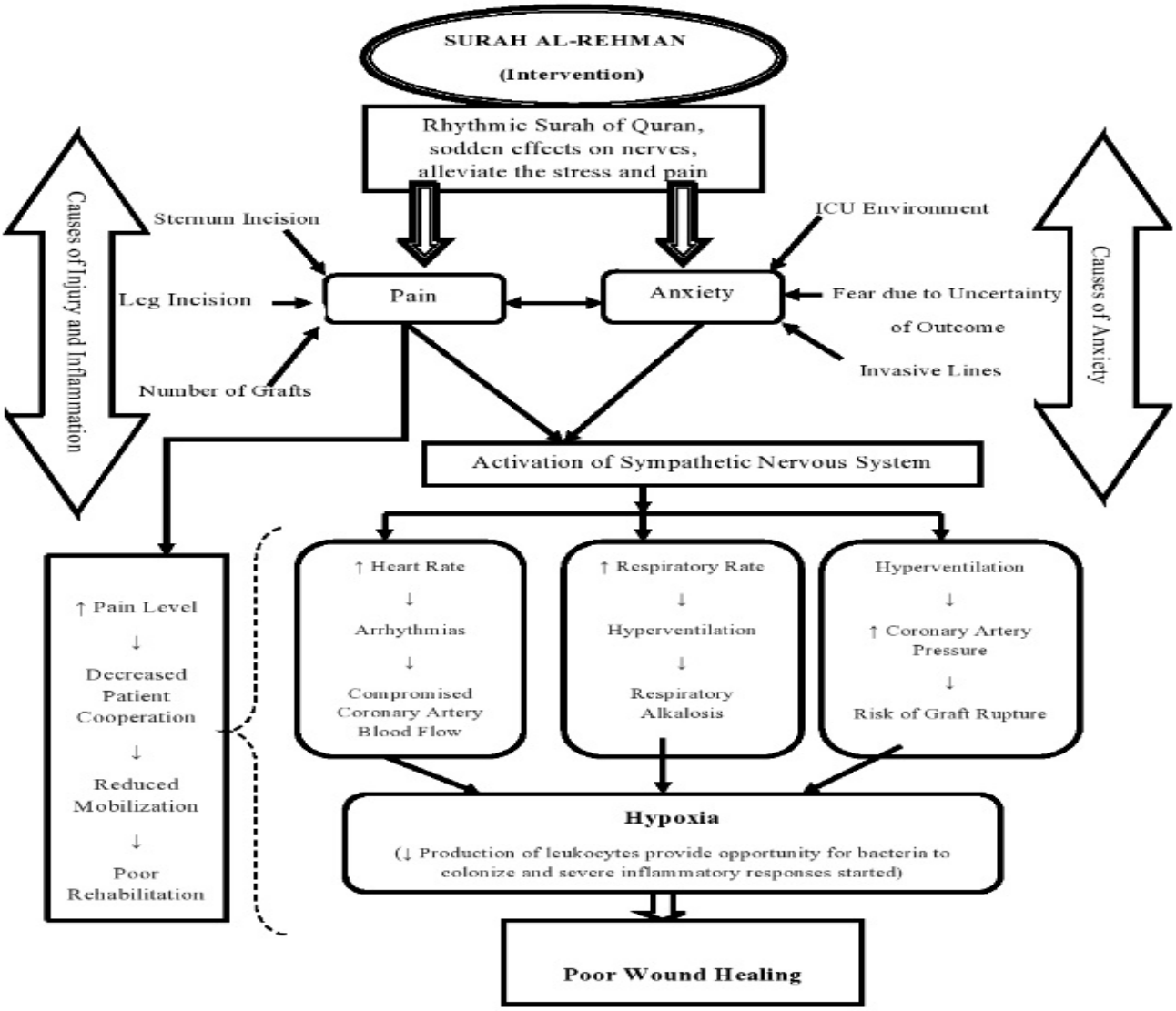

Figure 1: Summary of pain and anxiety complications

Methodology

The study protocol and the informed consent documents were reviewed and approved by the Ethical Review Board. Informed consent was taken from each participant under study. Participation in the study was voluntary. Participants had the right to withdraw from the study at any stage of data collection. All information about the study participants was kept under lock and key, and only the primary investigator was authorized to access it.

A quasi-experimental pretest and post-test interventional design was used in this study.

The study population consisted of post CABG adult Muslim patients while recovering from their surgery in the ICU. Patients were recruited from two tertiary care hospitals in Islamabad of the two, one is a private hospital that was denoted as hospital A and the other hospital, which is a public hospital, was denoted as hospital B. Data were collected from July to September, 2018. All post CABG patients who were admitted in the ICU during this

period met the inclusion criteria and provided informed consent, were recruited in the study. A non-probability convenient sampling technique was used to collect the data, considering the conventional rule for this pilot study, 60 patients were recruited. [13, 14] All Patients were Muslims, adults, awake and alert with GCS 15/15. Patients who have been extubated at least four hours ago, in the stable condition, and rated <7 on the pain scale were recruited. Patients with Mitral, Aortic or both valves replacement and those not willing to sign a written consent were excluded from the study.

Patients were selected through the facilitation of the head nurse of the ICU. The demographic information was taken from the patient's file. Surah Al Rehman recitation was the intervention for the current study. Patients were facilitated to listen Surah Al Rehman in the voice of the Qari Abdul Basit using Nokia A2 Mobile phone and a headphone (SPACER). with. The intervention took 21 minutes, which was repeated three times a day, in the morning at 0800AM to 1000AM, afternoon 1300 hours to 1430 hours and at night 2000 hours to 2200 hours.

A self-developed structured checklist was used for data collection. The checklist was written in the English language, which was filled by the primary researcher. The first part of the checklist was for demographic information of the study participants like age gender, marital status, professional qualification and reading about the Quran. The second part of the checklist was for clinical variables like primary diagnosis, number of grafts during CABG, chest drain insertion, Co-morbidities and pain level of the patient. Third part of checklist was for vital sings of the patient including heart rate, systolic, diastolic blood pressure, respiratory rate, pain level, and oxygen saturation level.

The pain scale was rated in consultation with the patient, whereas the respiratory rate was measured manually for full one minute. Heart rate, Oxygen saturation (SPO2), Systolic and Diastolic BP were observed from the cardiac monitor. While the first and 2nd part of the check list were completed after obtaining consent from the patient, information in the 3rd part of the check list were recorded thrice before and after the intervention.

Statistical Analysis was performed in SPSS software version 20. The descriptive statistics were applied to the demographic variables. In inferential statistics, Repeated Measures ANOVA was run to assess the overall effect of an intervention for three times. Moreover, a Bonferroni pairwise test was applied to compare the mean difference at three different time points.

Results

Overall, 60 patients participated in this study. The participants mean age was 55.95 +8.36 years. The Majority (76.6%) of them were male; all participants were married. Nearly one fourth of the participants were illiterate while most of them have had Middle and Matric level education. Almost all of them (90%) could read the Quran but none of them was Hafiz-e-Quran (people who have memorized the Quran).

Most of the participants (98.3%) have had triple vessels coronary artery disease, and they (76.6%) had three grafts. All of them had a chest drain. With regards to co-morbid, Hypertension (58.3%) and Diabetes Mellitus (45%) were the most common conditions.

Effect of intervention on Outcome Variable: Pain Level

The mean difference of pain level pre and post-intervention is shown in Table 1. Accordingly, the level of pain had reduced after the intervention as compared to pre intervention. Albeit with the slight variations at each time, the mean difference was statistically significant (At time 1, 2 and 3 $p<0.001$). Moreover, the results of Repeated Measures ANOVA also determined an overall significant decrease in the pain level ($F (3.19, 184.24) = 49.28$, ($p<0.001$).

Table 1: Comparison of Pain Level at Pre and Post Interventions

Time	1	2	3
Pre-Intervention Mean ± SD	3.25 ± 1.66	2.50 ± 1.34	2.41 ± 1.22
Post-Intervention Mean ± SD	1.90 ± 1.44	1.38 ± 1.15	1.13 ± 1.19
Difference	1.35	1.11	1.28
P-value	<0.001	<0.001	<0.001

[An overall significant decrease in the pain level $F (3.19, 184.24) = 49.28$, $p<0.001$) *]

Table 2: Comparison of Oxygen Saturation Level at Pre and Post Intervention

Time	1	2	3
Pre-Intervention Mean ± SD	95.73 ± 3.32	94.28 ± 8.63	95.28 ± 2.90
Post-Intervention Mean ± SD	96.65 ± 2.72	95.13 ± 9.17	96.63 ± 2.39
Difference	-0.97	-0.85	-1.35
P-value	0.02	<0.001	<0.001

[An overall significant increase in Oxygen Saturation level (F (1.30, 254.24) = 0.23, p= 0.01)] *

Table 2 illustrates the mean difference of oxygen saturation level pre and post intervention. Hence, the level of oxygen saturation increases post-intervention as compared to the pre-intervention. Though with the slight similarity at each time, the mean difference was statistically significant (Time 1 p=0.02, Time 2 p<0.001 & Time 3 p<0.001). Likewise, repeated measures ANOVA also revealed an overall significant increase in Oxygen Saturation level (F (1.30, 254.24) = 0.23, p=0.01).

Table 3: Comparison of Respiratory Rate in Pre and Post Intervention

Time	1	2	3
Pre-Intervention Mean ± SD	26.76 ± 5.23	27.28 ± 4.27	26.30 ± 3.98
Post-Intervention Mean ± SD	24.60 ± 4.34	25.30 ± 4.17	24.00 ± 3.70
Difference	2.16	1.98	2.3
P-value	<0.001	<0.001	<0.001

[An overall statistically significant decrease in respiratory rate (F (3.05, 495.85) = 14.62, p<0.001]

The mean difference of respiratory rate pre and post intervention is shown in table 3. The respiratory rate was decreased post intervention as compared to the pre intervention. Even though with the little change at each time, the mean difference was statistically significant at (At Time 1, 2 & 3 p<0.001). Similarly, Repeated Measures ANOVA also showed an overall statistically significant decrease in respiratory rate (F (3.05, 495.85) = 14.62, (p<0.001).

Effect of Intervention on Outcome Variable: Heart Rate

There was no significant decrease in heart rate post-intervention as compared to the pre intervention. Even though with very minimum variations at each time, the mean difference was statistically insignificant at time 1, 2 (p=1.0) and 3 (p=0.07). Correspondingly, Results of repeated measures ANOVA also showed an overall statistically insignificant decrease in Heart Rate (F (1.95, 449.55) = 2.08, p=0.13)

Effect of Intervention on Outcome Variable: Systolic Blood Pressure

Tough there was a slight decrease in the values of systolic blood pressure after the intervention as compared to the pre intervention, but no statistical change was detected (At time 1, 2 and 3 p=1.00) at each point. Similarly, repeated measures ANOVA also determined an overall insignificant difference in systolic blood pressure (F (2.81, 442.48) = 0.82, p=0.47)

Effect of Intervention on Outcome Variable: Diastole Blood Pressure

The mean difference of diastole blood pressure in pre and post-intervention was calculated. Though there was a slight increase in diastole blood pressure, but this increase was statically significant at time 1 (p=0.05). However insignificant at times 2 and 3 (p=1.00 & p= 1.00). But on the other side the Repeated measures ANOVA revealed an overall significant increase in diastole blood pressure (F (2.55, 747.58) = 2.95, p=0.04)

Discussion

Overall, Surah Al Rehman had shown statistically significant effects on the participants' pain level, oxygen saturation level, respiratory rate, and diastole blood pressure. The results of the current study confirmed the mitigation effects of Surah Al Rehman on the level of pain in CABG patients. The effects of other Quranic verses, prayers, and recitations on the pain level, have been reported in the literature by other researchers,[15] Fatemeh et al.[11],[16] Beiranvand, et al.[15] found that the pain level was reduced significantly after the pray meditation ('Ya man esmoho davaa va zekroho shafa, Allahomma sale ala mohammad va ale mohammad') in the intervention group as compared to the control group. Likewise, a randomized control study conducted by Fatemeh et al.[16] among ninety

post-surgical patients, found that recitation of the word 'Allah' was effective in decreasing pain after orthopedic surgeries. Similarly, Nasiri et al.[17] reported that recitation of the word 'Allah' had significantly reduced pain in post CABG patients. Although the above-mentioned studies were based on a small sample size, their findings were consistent with the findings of the current study. Post CABG patients may experience pain a few months after their surgery[18], which may interfere with their rehabilitation to normal life activities. Given the findings of the current study, nurses should encourage Muslim patients for listening to the recitation of Surah Al Rehman three times a day to relieve the post-surgical pain. As an alternative use of pharmacological agents in controlling pain, this is a cost-effective intervention, and which has no side effects. Moreover, most people have access to smart phones and on which Surah Al Rehman can be easily downloaded.

The current study found that listening to Surah Al Rehman's recitation had increased the oxygen saturation level in post-CABG patients. A similar effect has been reported by Mirzaein et al.[9] where the intervention was the recitation of Surah Yasin in unconscious patients. Likewise, Mansouri et al.[8] had found that the recitation of Surah Yousaf significantly increased the oxygen saturation level in semi-conscious patients with GCS 8-10. However, Awa [12] found no change in oxygen saturation level after the recitation of Surah Al Fatehah and Surah Yasin in mechanically ventilated patients, which could be due to the sedative effects of medications on the respiratory status of the patients. In the light of above studies, it can be inferred that listening to Quranic recitation can have a relieving effect on the patients breathing and oxygen saturation unless the patient breathing is controlled mechanically, and the patient is kept on sedatives.

While looking for the effect of the intervention on respiratory rate, the results of the current study revealed a significant effect of intervention in decreasing the respiratory rate of post CABG patients. These findings are consistent with Mansouri et al.[8] But, contrary to the findings of other researchers [9, 12] who demonstrated no effect of Quranic Surah recitation on the respiratory rate. As noted in the previous section, this difference could be due to the patient's conscious level and nature of breathing as compared to the current study, both previous studies [9, 12] consisted of unconscious mechanically ventilated patients (Spontaneous versus mechanically controlled). Hence, the effect of Surah Al Rehman can be witnessed in conscious patients to reduce their work of breathing and consequently improving the oxygen saturation level.

The current study has revealed no significant effect of Surah Al Rehman on the patients' heart rate but there was some change in the pre and post values. These findings are in contrast with other studies [8,9, 12] where the researcher reported a decrease in the patients' heart rate after the intervention. In the current study, no change in heart rate was deemed irrelevant with the decrease in respiratory rate after intervention because of the biological plausibility. Therefore, the current study findings suggest that more research work is needed to find out the significant relationship between Surah Al Rehman and heart rate.

In this study, the recitation of Surah Al Rehman had no effect on systolic blood pressure. These findings are in line with the study of Awa[12] where the recitation of Surah Al Fatiha and Surah Yasin was the intervention. In contrast, Mirzaeian et al.[9] in their study, found that the recitation of Surah Yasin had decreased the patient's the systolic blood pressure. Similarly, Monsouri et al.,[8] also reported that the recitation of Surah Yousaf had decreased systolic blood pressure of the patients. These findings provide an inclination that Surah Al Rehman did not have any effect on stable patients' systolic blood pressure as compare to other studies [8, 9] where Quranic Surah were different and patients' condition was unstable like unconscious and mechanically ventilated patients admitted with the medical diagnosis while the current study patients were the post CABG patients.

The current study findings have revealed the increase in diastolic blood pressure of the study participants after the recitation of Surah Al Rehman. These findings are opposite to the results of Mirzaeian et al.[9] and Monsouri et al.[8] studies where the diastole blood pressure had decreased after the intervention in patients with low conscious levels. However, Awa[12] found no change in the diastole blood pressure of the mechanically ventilated patients after the recitation of Surah Al Fatiha and Surah Yasin. Hence, Surah Rehman may be helpful in relaxing the heart for its better perfusion for the hemo-dynamically stable patients after CABG surgery.

In the conclusion of the above discussion there was a significant effect of Surah Al Rehman on the pain level, oxygen saturation level, respiratory rate and diastolic blood pressure in post-CABG patients however, there was no change in heart rate and systolic blood pressure.

This study was only limited to Muslim patients, so the findings cannot be generalized to Non-Muslim patients. This was only a pilot study with 60 patients so the findings should be generalized with caution. The researcher applied the intervention and collected the data before and after the intervention since this study was undertaken as a Master thesis, the researcher and thus, the risk of researcher bias cannot be excluded.[19] Replication of this study with large a sample size and using RCT is recommended.

Conclusion

The findings of this study indicated that Surah Al Rehman was an effective non-pharmacological intervention to decrease the post-surgical CABG patients' pain level and respiratory rate while improved the oxygen saturation level among CABG patients. Moreover, this non-pharmacological intervention has no cost and no side effects.

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ORIGINAL ARTICLE

Effect of parental relationships on stress levels of students in a medical college

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A B S T R A C T

Introduction: Multiple studies have been conducted on the theme of stress faced by medical students due to the load of medical education and lack of adequate stress coping skills which may affect the students variedly.

Objective: To critically assess stress levels in medical students of Shifa College of Medicine (a private medical college in Islamabad, Pakistan) and the quality of relationship between students and parents, thereby studying a relationship between the two.

Methodology: A cross-sectional study was conducted among the students of Shifa College of Medicine. A sample size of 315 students filled a pretested student stress questionnaire, which was made using the student life stress inventory survey consisting of 34 questions. Data was then analyzed using SPSS version 23.

Results: Increased levels of stress were found to be common among medical students with a prevalence of 53.3% among our study group. A total of 65.7% students face stress due to the increased expectations of their parents. There was a positive correlation ($p<0.05$) between stress faced by medical students and their relationship with parents. Academics, lack of recreational time and high self-expectations were also major contributors to student stress.

Conclusion: It can be concluded that there is a positive relationship between parental involvement and medical student stress at Shifa College of Medicine, which manifested in the form of excessively high parental aspirations, leading to adverse effects on the academic, social and personal life of a medical student.

Keywords: *Stress, medical students, parental involvement*

Introduction

Stress is defined as the body's non-specific response to any demand or change in the environment.[1] Various studies[2,3] have been performed to show incidence of stress among students in different medical colleges. Each showed a different level of stress among the participants.

In some analyses,[4,5] albeit intuitively, parental involvement has been operationally defined as parental aspirations for their children's academic achievement and parents' their conveyance of such aspirations to their children. Parental involvement plays a pivotal role in the academic and personal life of a student.[6] A huge workload[7] coupled with high parental expectations can put a lot of burden on the mental health of a student.

The degree of parental attachment of the student also determines the effect parental expectations have on a students' mental well-being.[8] Adolescent-parent attachment has special effects on reasoning, social and emotional life of the student.[9] Secure attachment is linked with fewer psychological health difficulties, and improved societal skills and coping strategies. Insecure attachment is related to anxiety, stress, depression and personality disorders. So, one of the factors to decrease stress is attachment.[10]

However, while such researches have been conducted in Pakistan and specifically, Islamabad, we noticed that not many linked the amount of stress to the relationship of a participant with his/her parents. Henceforth, the reasoning of this research is to appraise the relationship between parental attachment and stress in students of Shifa College of Medicine.

We aimed to critically assess stress levels in medical students at Shifa College of Medicine and to examine the different areas of stress faced by student, comprised of four categories. These categories consisted of stress faced due to academic factors, stress faced due to social factors, stress attributed to personality traits and a category to determine the quality of the student/parental relationship. This would help determine any correlation between stress faced in three of these categories with the trait assessed in the final category, namely, the relationship between participant and guardian.

Through this study we hope to raise awareness to the problem presented as stress, and how parents can work with their children to reduce this, making life better for both parties and ensuring a brighter future for the children involved. This would enable the university to have a better understanding of the problem and they would be in a better position to develop action plans to help their students to manage their stress, paving the path to ultimately achieving the university's goal of producing excellent and high-quality medical graduates.

Methodology

A cross sectional study was conducted among the students from years 1-5 studying in Shifa College of Medicine, Islamabad, Pakistan.

A pretested student stress questionnaire was used to assess the effect of parental relationships on student stress. Some questionnaire items were borrowed from a validated student life stress inventory questionnaire developed by Gadzella BM in 1994 [11] which was also later adapted in 2012.[12] Our questionnaire consists of 34 questions with answers based on a 5-point Likert scale, as well as two (Yes/No) questions asking about the current state of the participant's parents.

For the Likert scale questions, the students responded by making a choice from the five possibilities provided. These possibilities were divided into two as follows: the statements portraying positive feelings were scored in the following ways: Strongly agree – scored five points, agree – scored four points, Neutral – scored three points, disagree – scored two points, strongly disagree – scored one point. On the other hand, statements portraying negative feelings were scored in the following manner: Strongly Agree – scored one point, agree – scored two points, Neutral – scored three points, Disagree - scored four points, strongly disagree– scored five points.

A sample size of 315 students was calculated using the WHO sample size calculator. Simple random sampling was employed as the selection technique of the subjects ensuring that every student from each of the years (First – Fifth) had an equal chance of selection.

To ensure content validity, the questionnaire was given to the head of Department of Psychology in Shifa Tameer e Millat University (STMU) who examined the questions critically, based on which the researcher then modified the items and necessary adjustments were made. Data was analyzed using SPSS version 23.

Research Ethics Committee (IRB) approval was obtained before starting the data collection and debriefing done. A consent form was signed by the participants before filling the questionnaire who were allowed to ask any questions regarding the research and had the autonomy to withdraw from the research if they had to. The respondents were assured of their anonymity and confidentiality by asking not to write their names on the questionnaire. The only personal information retained were the participant's gender, age and the year they currently study in.

Results

During the study 315 students completed the questionnaire. From these, 138 were females and 154 were males. However, no significant difference was found in the results from each gender.

We discovered that, among these students, a total of 212 out of 315 (67.3%) participants felt a significant amount of stress. Around 168 (53.3%) of the total sample size attributed high stress levels to have some sort of correlation with the quality of relationships with the parents and guardians. Another aspect of this research

consisted of determining major stressors felt across the most students. Frequencies for the highest felt stressors across all four categories are shown in Figure 1.

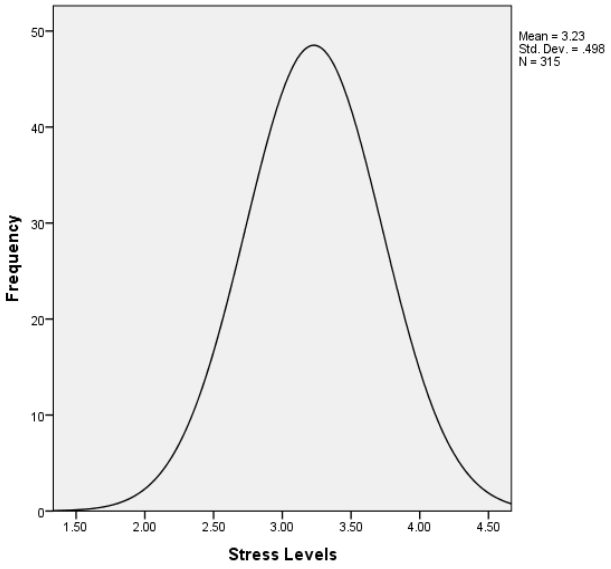

Figure 1: Frequency of average stress levels faced by students plotted along a scale of 1-5 (with 1 being the least stress and 5 being the most)

Through our survey, we realized that most students face stress due to the increased expectations of their parents to achieve good grades in their tests (65.7%) as shown in Figure 2. In the realm of personality traits, we discovered that many students possessed a tendency to procrastinate (74.9%). It was also discovered that students face most academic stress due to the overload from attempting too many things at once (76.5%). Major contributions to social stress were supplied primarily by the lack of holidays given to students (73.3%).

A Pearson correlation test (significance was valued at the 0.05) showed multiple correlations between stress levels in three different aspects of a student's life (Academics, Social and Personality) and stressors due to strained relationships between participants and their parents, as shown in Table 1. A negative correlation was obtained between good parental relationship and academic stressors with a p value of 0.733 and another negative correlation with personality traits (p = 0.23) was also found. It is worth noting that stress faced due to social aspects of a student's life is independent of their relationships with their parents, as shown in Table.1

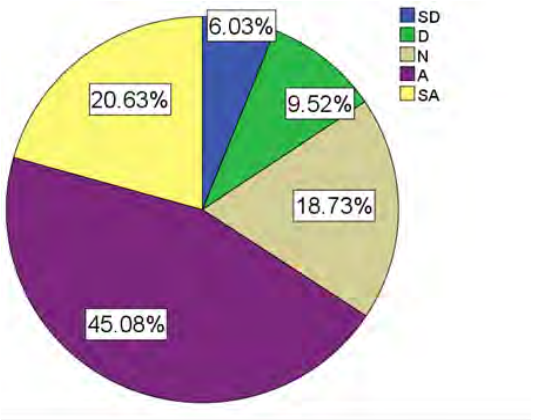

Figure 2: Frequencies of stress faced by students due to parental expectations. (SD – Strongly Disagree, D – Disagree, N – Neutral, A – Agree, SA – Strongly Agree.

A significant relationship between the students' inability to achieve desired grades and the amount of time parents could allow for the student to study was not found (p=0.679). Another study related stressor, that stemmed from the difficulty of the syllabus itself was not related to the decision of parents to force the students to join the medical field (p=0.340)

Table 1: Significance level of bad parental relationship.

Bad relationship with parents	p value
Stress due to academic reasons	0.002
Stress due to social reasons	0.000
Stress due to personality traits	0.003

In the students who had the tendency to worry a lot, there was no association of this trait with the parents listening and talking about their problems (p=0.300). However, this same parental stressor had a significant correlation with the students who underwent verbal or physical abuse by their peers (p=0.015). There were also significant correlations between various student and parental stressors which are shown in Table 2.

Table 2: Significance level of different stressors

Student and parental stressors	p value
My parents allow me enough time to study properly	0.000
Difficulties in covering a large syllabus	0.000
My parents expect me to excel in my exams	0.021
Inability to achieve desired grades	0.021
Small arguments with parents	0.000
Feeling incompetent	0.000
Provision of basic necessities by parents	0.013
Social unacceptance	0.013

Discussion

The present study confirmed the general impression that stress is common among medical students with a prevalence of 53.3% among our study group in the four categories: stress faced due to academic factors, social factors, personality traits and the quality of the student/parental relationship. Various studies have been done to approximate the number of students who feel a certain amount of stress, with some research listing it as being up to 78.19% of students.[2,13]

There was a significant relationship between student stress and parental expectations, which were found to be the major stressor in 65.7% of the students. These results are consistent with research carried out in Nepal[14] and United Arab Emirates.[15] A significant association between family problems and psychological morbidity has also been reported in similar researches.[16]

This study examined the effect of parental pressure on a medical student's academic activities, social life and personality traits. As mentioned previously, we have found that students who have better relationships with their parents' face decreasing stress in both academic and personal categories, as opposed to students who have a worse relationship with their parents. These students faced a significant amount of stress throughout all categories, Academic, Social and Personality traits. We also discovered that social stress faced by students was not affected even in students who had good relations with their parents. A few researches have related social stress to other factors, disregarding parental influence.

A p value of .021 was found in the correlation of students who face stress due to inability to achieve their desired grades, and also experience stress due to high parental aspirations, which coincides with the results of a study conducted in India.[17] The reason might be that students perceive their parental aspirations to be stressful, making them want to achieve the maximum, within a limited time period, which often causes stress among them.

Conclusion

From our study it can be concluded that there is a positive relationship between parental involvement and medical student stress at Shifa College of Medicine. In this study it manifested in the form of excessively high parental aspirations from their children to excel in their exams, which causes the student to feel a significant additional burden to the already high stress levels caused by the strenuous activities of a medical institution, leading to adverse effects on the academic, social and personal life of a medical student. This student distress, if not corrected or managed properly and within a proper time frame may lead to negative influences on the professional development of the student and will further have an adverse impact on their mental health.

Recommendations

Our study and its results highlight the need for prompt interventions in this regard due to the negative effects on the lives of medical students, as mentioned previously. Not only should parents be made aware of the aforementioned issue, but they should also be informed on how to alleviate some of the overall stress levels faced by a student. Well trained counselors should also be made available for the students to train them on various techniques for coping and management of stress and anxiety, as according to the student in question.

Limitations

The study was limited to a sample of students in Shifa College of Medicine. This is due to financial and time constraints. Consequently, the results of this study will not be generalized to all medical schools in Islamabad. Only students studying MBBS were considered, therefore, the

results cannot be applied to other fields pertaining to medicine.

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ORIGINAL ARTICLE

Impact of breast cancer awareness health campaigns on knowledge of female educationalists of Islamabad and Rawalpindi; an interventional study

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[1] Supervision, ideation, Final revision
[2] Conception, design, Data collection, drafting the article, references
[3] Data entry, Data analysis, interpretation of data, revising the article critically
[4] Conception, Questionnaire, data collection, revising the article critically, abstract writing
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A B S T R A C T

Introduction: Breast carcinoma is the leading cause of cancer in women worldwide. WHO statistics show 1.2 million new cases every year. Pakistan reports nearly 40,000 lives from Breast Cancer annually.

Objective: To evaluate existing awareness levels regarding breast cancer among female educationalists in twin cities and to counsel the participants about diagnostic tools such as mammographic-screening and breast self-examination

Methodology: The study design was an interventional community trial and was conducted on female teachers aged 30-60 years. Data was collected by a questionnaire, given before and after the interactive session to evaluate its impacts. SPSS Version 23 was used for data entry analysis. Descriptive statistics were used to calculate the quantitative and qualitative variables. McNemar's test was applied for this. P values less than 0.05 were considered significant.

Results: Total number of participants was 106 women with a median age of 43.3 years (range of age 31-54 years). Before intervening, 67 (63.2%) participants had no knowledge of mammographic-screening and 15 (14.2%) participants didn't know the definitive way of diagnosing it. 2 After intervention, mammogram was selected to be the definitive way of diagnosing breast cancer by 91 (85.8%) participants. 91(85.8%) participants would encourage close family and friends to get screened. 104 (98.1%) of women had become familiar with technique of self-examination, as compared to 63 (59.4%) before.

Conclusion: Misconceptions about risk factors, screening methods and diagnostic procedures were identified and elucidated. This encouraged participants to start performing regular self-exams and get mammograms.

Keywords: *Breast cancer, Breast self-examination, female educationists, mammography*

Introduction

According to the WHO, breast cancer numbers have been going up for years and it has been identified as the cancer with the highest female mortality.[1] Over the years there has been huge progress in the search for curative treatments and overall management of this disease. Studies have linked up to 40000 deaths in Pakistan every year to breast cancer.[2] Compared to India and Iran, the incidence rate is nearly two and a half times greater. Pakistan also reports the highest incidence rate in the entire South Asia at 69 per 10,000.[3] Even as the disease continues to affect lives of women across the country indiscriminately regardless of the social barriers. The

availability of medical resources has remained low due to sexual discrimination and societal norms that often actively discourages any talk about female centric health problems. The importance of awareness and early diagnosis can never be overstated.

A research, conducted to find the reasons behind the rise in the incidence of breast cancer in South Africa [3] and why some women were diagnosed late, drew a direct correlation between late diagnosis and poor outcome.[4] Hence, reiterates the importance of self-examination and early diagnosis. Disappointingly, a different study conducted in Bahawalpur, Pakistan, in 2015, found that only four women out of all the respondents had complete awareness about breast cancer.[5] Overall, the majority of them were deemed to have poor knowledge on this matter; an alarming situation in a country so lacking in health infrastructure. Our study was designed to gauge the knowledge and awareness of the female educators. It was also expected to provide an insight into the effectiveness of recent breast cancer campaigns and to highlight the degree of improvement in knowledge regarding breast cancers, pre and post counselling sessions.

Methodology

An interventional study was conducted among female educationalists employed in educational institutions of Islamabad and Rawalpindi, Pakistan. The objective was to determine the effectiveness of breast cancer campaigns and to raise awareness among them. Undergraduate institutions were mainly targeted for study purposes. Study researchers, between first to 31st of November 2019, conducted educational sessions with female educationalists. Total number of 106 women with a median age of 43.3 years (range of age is 31-54 years) participated in the study. They responded voluntarily to participate in this session regarding the basic knowledge about breast cancer and technique of self-examination after informed consent. This research is based on interventional community trials. Research team members under the supervision of the research committee of SIH constructed a structured questionnaire. It consisted of 36 questions. The questionnaires were validated and adjusted on two pilot lectures with 15 participants among each session. Data collected via a self-administered questionnaire was filled by the study subjects, prior to an interactive session with them to test their knowledge regarding breast cancer, its self-examination and screening. An interactive session was given which included knowledge about breast cancer and self-diagnostic techniques illustrated through videos and presentations shown by our female researchers to the study participants.

The study participants completed the questionnaire after the intervention to assess the effectiveness of breast cancer awareness session. The method employed for sample selection was "simple random sampling" and sample size calculated using WHO sample size calculator was 100 to 150. The lecturers used a standardized, culturally sensitive presentation that included the following topics: what is breast cancer, why necessary to raise awareness about breast cancer, breast cancer statistics in Pakistan, breast cancer risk factors, signs and symptoms, benefits of early detection, breast self-examination (BSE) training, how breast cancer is diagnosed, clinical breast examination and mammography, breast health national guidelines and treatment options. Inclusion criteria was females between ages of 35 to 55 and had to be an educationalist at a college or under-graduate level. Exclusion criteria was included male educationalists and female educationalists who refused to participate in the study voluntarily. The ethical approval of this study was granted by the IRB Shifa International Hospital. The participants were informed about the purpose of the study, and informed consent from the participants was taken and they were assured of complete participant confidentiality. The females diagnosed with breast cancer after self-examination were kept anonymous and advised to seek help. Only female researchers presented during interactions with the educationalists regarding the ethical considerations. The 36-item breast health knowledge questions were coded as correct or incorrect in SPSS Version 23. Due to ethical reasons, it was not possible to use any personal identification in some questionnaires, thus the pre-test and post-test questionnaires had to be analyzed as two separate surveys.

Results

Many misconceptions about breast cancer were cleared up after intervention e.g., knowledge about inheritance of breast cancer, diet and other factors affecting breast cancer, benefit of breast feeding against breast cancer

Table 1: Demographic Characteristics of Participants

Variables	Mean	S.D	Range
Age	43.3	7.2	31 - 54
		n	%
Education	Bachelors	34	32.1
	Masters	44	41.5
	PhD	14	13.2
	Diploma/Others	14	13.2
Marital Status	Single	23	21.7
	Married	70	66.0
	Separated / Divorced / Widowed	13	12.3

Our participants were female educators of Islamabad, their age ranged from 31 to 54 years, amongst them, most common education qualification was a Master's degree, followed by Bachelor's degree then PhD and Diploma/others.

Table 2: Knowledge about age at risk
(Pre intervention)

Which age group has the greatest chance of contracting the disease?	
Range	Frequency (%)
30-40	19 (17.9)
40-50	35 (33.0)
Above 50	24 (22.6)
Unsure	28 (26.4)
Total	106

These tables compare how often the participants performed breast self-examination. Our results show that of those women who did perform BSE, most performed BSE randomly and the rest were following the advised once a month routine.

Table 3: Knowledge about age most at risk
(Post intervention)

Which age group has the greatest chance of contracting the disease? (Post Intervention)	
Range	Frequency (%)
30-40	5 (4.7)
40-50	26 (24.5)
Above 50	75 (70.8)
Total	106

These tables compare the participant's knowledge regarding age group that is most at risk before and after intervention. Before intervention, only 22.6 % of participants correctly pointed out the age group that is at greatest risk of contracting Breast Cancer, where as a majority, 70.8%, correctly pointed out this age group post intervention.

Table 4: Breast Self-examination
(Pre intervention)

How often do you self-examine?	
	Frequency (%)
Random	24 (22.6)
Once a month	10 (9.4)
No comments	72 (67.9)
Total	106

Table 5: Breast Self-examination
(Post intervention)

How often do you self-examine?	
	Frequency (%)
Random	19 (17.9)
Once a month	15 (14.2)
No comments	72 (67.9)
Total	106

Table 6: why don't you self-examine?
(Pre intervention)

If not, why don't you self-examine?	
Options	Frequency (%)
I do not know how to do it	53 (50.0)
I feel scared about actually finding a tumor	19 (17.9)
No comments	34 (32.1)
Total	106

Table 7: Why don't you self-examine? (Post intervention)

If not, why don't you self-examine? (Post Intervention)	
Options	Frequency (%)
I do not know how to do it	53 (50.0)
I feel scared about actually finding a tumor	19 (17.9)
No comments	34 (32.1)
Total	106

These tables compared the various reasons why our participants did not perform BSE. The most common reason among those who did not perform BSE was a lack of knowledge about proper technique, followed by the fear of actually finding a tumor.

Table 8: Diagnosing Breast Cancer (Pre intervention)

Which of the following, do you think is the most definitive way of diagnosing Breast Cancer?	
Options	Frequency (%)
Mammogram	44 (41.5)
Breast Ultrasound	14 (13.2)
Breast MRI	10 (9.4)
Biopsy	23 (21.7)
Unsure	15 (14.2)
Total	106

Table 9: Diagnosing Breast Cancer (Post intervention)

Which of the following, do you think is the most definitive way of diagnosing Breast Cancer? (Post Intervention)	
	Frequency (%)
Mammogram	91 (85.8)
Breast Ultrasound	0 (0.0)
Breast MRI	0 (0.0)
Biopsy	5 (4.7)
Unsure	10 (9.4)
Total	106

These tables compared the participant's knowledge about the definitive ways of diagnosing breast cancer. Of the results before intervention, only 41.5% of participants correctly chose Mammogram as the most definitive way of diagnosing breast cancer, however after intervention this rose to 85.8%.

Table 10: Knowledge about Mammography (Pre intervention)

If yes, then what is your source of knowledge about Mammography?	
Options	Frequency (%)
Social media	20 (18.9)
Posters/Print media	9 (8.5)
Television/Movie	9 (8.5)
Someone talked to me about it	5(4.7)
I attended a seminar/Educational conference.	5 (4.7)
Someone close to me was diagnosed with breast cancer	19 (17.9)
Unsure/No comments	39 (36.8)
Total	106

Table 11: Knowledge about Mammography (Post intervention)

If yes, then what is your source of knowledge about Mammography? (Post intervention)	
Options	Frequency (%)
Social media	20 (18.9)
Posters/Print media	15 (14.2)
Television/Movie	5 (4.7)
Someone talked to me about it	5(4.7)
I attended a seminar/Educational conference.	42 (39.6)
Someone close to me was diagnosed with breast cancer	19 (17.9)
Unsure/No comments	0 (0.0)
Total	106

Our results show that before intervention social media was the prime source of information about Breast Cancer for the participants and only 4.7% of participants had ever attended a seminar/educational conference regarding the topic of Breast Cancer.

Table 12: Consider getting screened

Will you ever consider getting screened?	
Options	Frequency (%)
Yes	58 (54.7)
No	23 (21.7)
Don't Know	5 (4.7)
Not Answered	20 (18.9)
Total	106

In this table we can see that a majority of the participants would consider getting screened which is an encouraging finding.

Discussion

Our results show that many female educationalists have a basic understanding of breast cancer but lack the knowledge of its risk factors and the importance of breast self-examination. Over 80 (77.4%) participants in this study had heard about breast self-examination, which was similar to the Egyptian study that reported 63.4% of participants had heard about breast self-examination.[6] However relatively few (40.6%) participants knew the correct technique of breast self-examination. Similarly, a study conducted among women in Ondo state, Nigeria Makanjuola et al., (2013) reported that only 22% of participants understood what BSE was.[7] We found that of the participants who performed breast self-examination, only a few (29.4%) had correct knowledge regarding the recommended frequency (monthly) to perform breast self-examination. However, the study among female university students in Egypt reported that only 8.8% of participants knew the appropriate time to perform breast self-examination.[6]

A concerning finding in our study was that few (32.2%) participants performed BSE, and most of the participants (67.8%) rarely performed breast self-examination. This finding was consistent with that of a study among female university students in Jordan that reported 11% of participants performed breast self-examination.[8] The two most common reasons for not performing breast self-examination given by participants in our study were “do not know how to perform breast self-examination” and “scared of actually finding a tumor”. The study involving Egyptian students reported similar reasons for not performing BSE, such as “did not know how to perform BSE” and “lack of interest”.[6]

An encouraging finding in our study was that many stigmas and questions about breast cancer were answered, and many participants were ready to encourage their family and friends to get screened for breast cancer and to perform regular breast self-examination.

In our study, most of the participants were knowledgeable about certain risk factors (environmental pollutants, family history, age) and their associations with breast cancer. Most (78.6%) could identify the age group at greatest risk of developing breast cancer (after age 50) which is similar to a study done in Iran which identified the mean age of developing breast cancer to be 48 years of age.[9]

Conclusion

The rise in number of breast cancer cases is, fortunately, accompanied by increasing cognizance amongst the populace. Almost all study participants had previously heard about the disease and 77% responded positively when questioned about awareness regarding basic self-examination. Word of mouth and social media were credited for this increased awareness and identified as the most effective mediums for future campaigns.

The most worried finding was that 21.7% people refused the possibility of a future screening. The fear of being diagnosed positive for the disease was reported to be the primary cause of this refusal. It is paramount that future campaigns focus on reducing this fear and work on increasing the number of people willing to get screened.

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REVIEW ARTICLE

Cardiac implantable electronic device related chest pain: A focused review

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A B S T R A C T

More than 600,000 patients undergo cardiac implantable electronic device (CIED) implantation in a year, which comprise of pacemakers, implantable cardioverter defibrillators, and cardiac resynchronization therapy devices (CRT). The most common symptom experienced after a CIED implantation is chest pain. In this review, we describe CIED implantation and associated complications causing chest pain.

Keywords: *Cardiac implantable electronic device (CIED), chest pain*

Introduction

More than 1.5 million patients undergo cardiac implantable electronic device (CIED) implantation in a year.[1] These CIED implantations comprise cardiac resynchronization therapy devices (CRT), permanent pacemakers, and implantable cardiovascular defibrillators.[2] With the advent of modern equipment and standard-of-care in placement techniques, the device surgeries are considered safe. However, these procedures are not without risk, as several complications can occur after device implantation either acutely or in a delayed setting[3,4] All the complications can differ in etiology, morbidity, and mortality but most of them have a common presentation of chest pain.[5] The implantation procedure can itself cause chest pain so it is imperative to differentiate the etiology of chest pain, especially acute coronary syndrome (ACS). Interpreting an electrocardiogram in a ventricular paced rhythm is sometimes difficult as it can hide or mimic ST-T changes in ACS. The modified Sgarbossa criteria can be applied for diagnostic accuracy in these patients.[6] As a result, it is paramount in diagnosing the cause of chest pain after device implantation. In this review, we will discuss various causes of chest pain after CIED surgery.

Evaluation of chest pain after CIED implantation

Like every surgical procedure, lead placement and device implantation can stimulate numerous nerve endings and by itself produce chest pain, which can occur during the procedure, in the postoperative period, or well after CIED implantation. Hence, the etiology of chest pain can be divided by the time of occurrence: (i) chest pain during the procedure (ii) immediate post-procedural chest pain (iii) delayed presentation of chest pain.

i. Chest pain during the procedure:

A moderate sedation is given during CIED implantation because patients undergoing such procedures are usually elderly and have multiple co-morbid conditions.[7] This limits the use of proper analgesia and sedation to limit the adverse effects of sedatives and anaesthetics and imparts an important role of local anaesthesia for pain control. If local anaesthesia is not given adequately, patients might experience pain during different steps of device implantation. Even with sufficient

local anaesthesia, only subcutaneous tissue is effectively anesthetized and patients may experience sharp pain when deep tissue or bone is being manipulated.[8] Muscles are especially prone to pain having sutures during lead or device fixation or cauterization for inadvertent bleeding. Hence, quick vascular access is important to minimize pain and other complications of CIED implantation. Most of the physicians at our institute use a sub clavicular approach for subclavian vein access but one of our study has shown the supra-clavicular approach to be non-inferior and time-efficient in temporary transvenous pacing.[9] Hence, we prefer a supraclavicular approach in CIED surgeries as well.

One of the most dangerous complications during CIED surgery is pneumothorax and hemothorax.[10] These complications are always evaded by implanting physicians because they can increase morbidity and mortality. One way to avoid these complications is by a 'buddy' microneedle puncture after contrast venography to identify the veins.[11] Similarly, ultrasound-guided access can be used to identify veins, and positioning of the patient according to their anatomy can help the physician in gaining access. The contrast tends to dilate and engorge the veins, so some physicians like to inject 2ml of contrast for easier venous access. Although CIED surgeries are done meticulously, sometimes pneumothorax does happen. Even when the vein is punctured outside the thorax, a pulmonary bleb formed due to chronic obstructive pulmonary disease can inadvertently cause pneumothorax upon entry.[12] Any air entry during venous puncture should alert the physician about a chance for pneumothorax and the syringe attached to the needle should be airtight. Otherwise, it can give a false perception of air aspiration into the syringe. Any development of chest pain, hypoxia, or cough can be a sign of evolving pneumothorax and during this situation, prompt fluoroscopy can help in identifying the cause of hemodynamic instability. Apart from pneumothorax, multiple venous or arterial punctures can cause mediastinal bleeding. Any bleed in the thorax during CIED implantation can cause acute chest pain. This can present as a diffuse pain that radiates to the back due to mediastinal reflection.[13] Sympathetic stimulations can cause tachycardia and hypotension, depending upon blood loss. There is a high chance of subclavian arterial puncture causing mediastinal bleed.

Hence, some physicians prefer axillary vein puncture at the level of the first rib because it allows for manual compression if a hematoma is suspected.[14] After securing the central venous access, it is imperative to advance the guidewire below the diaphragm to ensure the placement within the right heart rather than the arterial side before sheath insertion. In this way, the chance of mediastinal bleeding can be minimized. In elderly patients, vessels are usually tortuous and the advancement of a guidewire and sheath should be very slow.[15] If there is any resistance, further advancement should be done under fluoroscopic guidance.

In addition to mediastinal bleed, it is possible that during the procedure a patient suffers an acute pericardial bleed leading to pericardial effusion or tamponade.[12] These patients typically have chest pain along with hemodynamic instability and cardiogenic shock.[16] As with the pericardial reflection, the chest pain can radiate to the shoulder blades of the scapula. Additionally, it can be due to the rubbing of the pleura with the pericardium.[17] Perforation can occur at any level and superior vena cava, right atrium, right atrial appendage, right ventricle, and coronary sinus have been known to perforate during procedures[3,18,19] When there is suspicion of pericardial effusion, transthoracic echocardiography is the imaging modality of choice, which can be carried out promptly so an appropriate treatment is undergone promptly. Lateral movement of the pericardium under fluoroscopy is another useful test to check for pericardial effusion. In this case, urgent Pericardiocentesis can be life-saving and lead extraction may be indicated depending on the clinical situation.

ii. Immediate post-procedural chest pain

As a consequence of every surgical procedure, there is some post-operative swelling at the incision site. This typically responds to simple analgesics or cold compression. One other cause can be a superficial placement of the subcutaneous device leading to a significant chest compression and lateral displacement of the device causing axillary nerve compression and entrapment.[20,21] There is also a rare occurrence of allergic reactions to CIED material like chromium, titanium, and nickel.[22] As the patients are advised to restrict right arm

movement after CIED surgery, it can produce shoulder pain similar to adhesive capsulitis.

As discussed in the previous section, pneumothorax, haemothorax, and pericardial effusion can produce symptoms of chest pain after a CIED procedure. This typically happens due to a discontinuity of the pleural or pericardial membrane by lead perforation.[23] If there is clinical suspicion of lead misplacement or dislodgement, lead revision would, in most cases, take care of the chest pain promptly.

Any procedure, even a minor surgery elevates stress levels and anxiety. Some patients can develop Takotsubo cardiomyopathy as a consequence. The incidence, however, is still unknown. Clinically, the patient may experience angina, shortness of breath, and palpitations owing to new-onset arrhythmias. Troponin levels are raised and transthoracic echocardiography will show apical ballooning with sparing of the basal septum.[24] Left heart catheterization shows unobstructed coronaries. The etiology of stress cardiomyopathy is not clear, although its pathophysiology is apparent in CIED surgeries. It can be induced secondary to the stressful events leading to device implantation, sedation and other medications, dyssynchronous pacing, or the CIED procedure itself.[25]

A rare cause of chest pain in these patients can be diaphragmatic pacing by capture of the phrenic nerve.[26] This can manifest as hiccups or chest discomfort, manifesting in a certain posture. In CRT, coronary sinus lead is placed in the posterolateral or lateral branches which brushes off the lateral wall of the ventricle and this lead can capture phrenic nerve leading to diaphragmatic contractions.[27] The right ventricular lead, on the contrary, cannot pace the diaphragm unless there is lead-induced ventricular perforation. It is usually fixed with lead revisions.

iii. Delayed chest pain

Most of the patients with delayed onset chest pain present with some surgical site problems. Pain after surgery usually settles within one week. However, some people have increased sensitivity and a low pain threshold. Hence, a sizable percentage complain of prolonged chest discomfort. Other conditions include superficial placement of the device, nerve entrapment, hematoma, erosions, dehiscence, or infections.[20] The etiology of pain is the deciding factor towards lead revision or reopening the device pocket. A major cause of lead revision is perforation which can be delayed secondary to CIED implantation. It is uncommon as compared to acute perforations and usually presents with vague clinical symptoms. Hence a high degree of suspicion should be maintained and the help of imaging modalities like X-ray and echocardiography should be advised promptly. These patients often require a multidisciplinary approach including electrophysiologists and cardiothoracic surgeons.[28]

In addition to an iatrogenic cause of chest pain, some patients have underlying coronary artery disease, and pacing can induce angina by elevated heart rate.[29] In certain instances, dual-chamber pacemakers induce high atrial rates and cause ventricular pacing. Although pacemakers are programmed to minimize right ventricular pacing, sometimes it is inevitable and results in demand ischemia.[30] In the presence of subclinical ischemic heart disease, it can lead to classical angina. This phenomenon can be diagnosed by alternating the pacing rate and reprogramming the device to minimize right ventricular pacing can relieve the anginal symptoms, and subsequent revascularization for underlying coronary artery disease should be planned for complete resolution of chest pain.[31]

In a subset of patients with CRT implantation, a delayed onset, pleuritic chest pain can be precipitated, similar to Dressler's syndrome. Differentiating feature from other types of pericardial entity is that it does not produce pericardial effusion or tamponed. This syndrome is named post-cardiac injury syndrome (PCIS) and it refers to heterogeneous autoimmune-mediated conditions of pericarditis and myocarditis.[32] There are no validated diagnostic criteria but patients suffering from PCIS seek medical care due to chest pain in 80% of the cases. Other clinical presentations include shortness of breath and fever. The initial trigger for PCIS seems to be a break in pericardial space in combination with blood entering the pericardium. There is evidence of elevated anti myocardial antibodies and the incidence of PCIS after cardiothoracic procedures. Taking the latency period between cardiac injury and favourable response to anti-inflammatory drugs, the hypothesis of autoimmune-mediated pathogenesis seems legitimate.[33]

Most of the patients can bear right ventricular pacing without any noticeable side effects while others may

develop significant chest pain, irrespective of coronary artery disease.[34] Although the principal pathophysiology is unclear, several hypotheses exist in this view: asynchronous ventricular contraction due to abnormal septal motion, activation of neurons for interception ventricular pacing, and micro vascular ischemia. In view of current evidence, treatment of these patients is tough, but CRT therapy or His bundle pacing can be considered for a favourable response.

Conclusion

A significant proportion of patients that undergo CIED surgeries will have device-related chest pain with various etiologies depending upon the time of occurrence. The most common cause for CIED-mediated chest pain is surgical site pain. However, life-threatening complications like acute myocardial infarction or pneumothorax should be taken into account when investigating chest pain in these patients because prompt diagnosis and treatment are needed for better outcomes.

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REVIEW ARTICLE

Emerging role of chondroitin sulfate based nanocarriers in improving the therapeutic outcome of NSAIDs in the treatment of osteoarthritis through the TDDDS

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Author`s Contribution

[1] Literature search and analysis on nanocarriers, writing
[2] Literature survey for chitosan
[3] Literature survey of inflammatory pathway

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A B S T R A C T

Osteoarthritis is characterized by joint destruction followed by severe inflammation caused by variety of proinflammatory mediators released due to upregulation of nuclear translocation of nuclear factor (NF-kB). Current treatment involves chronic administration of non-steroidal anti-inflammatory drugs (NSAIDs) that is associated with bewildering array of systemic adverse effects. Transdermal drug delivery system address challenges of systemic toxicities but toxic chemical penetration enhancers limit its utility. Novel drug delivery system explores the potential of bio-inspired materials for designing of safe and effective carriers that specifically deliver drug to site of action with enhanced transdermal penetration of the drug. Chondroitin sulfate, a biopolymer that mimic extracellular matrix, binds specifically with its overexpressed receptors (CD44, RHAMM and ICAM-I) at inflammatory site, biodegradable and possess intrinsic anti-inflammatory properties. These attributes render chondroitin sulfate an ideal carrier for the drug delivery in osteoarthritis. Chondroitin sulfate based nanocarriers serve as a potential drug delivery system that not only deliver anti-arthritis drug through the skin but also produce synergistic effect to improve therapeutic outcome. In this review, molecular mechanism of intrinsic anti-inflammatory effects of chondroitin sulfate in osteoarthritis is discussed in detail. Moreover, potential of chondroitin sulfate to perform dual role of therapeutic agent as well as serve as nanocarrier in transdermal drug delivery for the treatment of osteoarthritis is elaborated.

Keywords: *Osteoarthritis, Bio-inspired polymer, chondroitin sulfate, transdermal drug delivery system (TDDDS)*

Introduction

Osteoarthritis is known as one of the most disabling disease worldwide and current therapy for the management of this chronic disease is not free from adverse events. Patients not only suffer from the devastating effects of the disease but also have to bear bewildering array of adverse effects allied with non-specific systemic delivery of therapeutic agents.[1] Non-steroidal anti-inflammatory drugs (NSAIDs) are the first line drugs that are widely utilized for the pain management in osteoarthritis. Arthritis patient requires chronic administration of these drugs that leads to GI ulceration and bleeding after oral administration. Parenteral administration of NSAIDs is invasive and leads to cardiovascular and renal complications. Intra-articular injections reduce systemic toxicities but causes necrosis at chronic site of administration. Mostly NSAIDs have short plasma half-life, therefore required frequent administration that reduced patient compliance.[2] Targeted drug delivery system can be designed to address the challenges of systemic toxicities. Drug delivery carriers for targeted delivery in osteoarthritis can be fabricated by taking the advantage of anatomical physiology of inflamed

area (passive targeting) or utilizing homing devices or ligands to specifically bind with target site receptors (active targeting).[3,4] Novel route of drug administration with sustain and targeted delivery aid in reducing systemic toxicities. Transdermal drug delivery system (TDDS) aimed to deliver drug through the skin into systemic circulation. Potential advantages of TDDS includes controlled drug release, reduced systemic adverse effects, bypass first pass effect, prevent GI bleeding and ulceration. Therefore, for chronic pain management, delivery system for NSAIDs must provide targeted and control release of medicament for prolong period of time. Transdermal formulations provide targeted and sustain release of medicament while minimizing systemic adverse effects. Transdermal administration of NSAIDs is advantageous because this route alleviates associated GI complications. Drug delivery through the skin is non-invasive. Sustain release omits necessity of frequent administration. These benefits ultimately improve patient compliance. Thus, these favorable advantages depict the importance of transdermal route as a suitable alternative for chronic therapy.[5]

For TDDS, active ingredient diffuses through the multiple layers of the skin which act as a barrier for the entry of any antigen. Physicochemical properties of the therapeutic agent predict its ability to pass through the skin barrier. Low molecular weight drug with high lipophilicity can easily cross this barrier. To achieve minimum effective concentration in plasma, skin permeability of the active ingredient is an important parameter. Limited skin permeability of many drugs posed a great challenge in designing transdermal drug delivery system. Variety of techniques are employed to enhance skin permeability of drugs by reversibly disrupting the skin barrier by interaction with skin lipids. These techniques include use of chemical penetration enhancer, physical penetration enhancing techniques and nano-cargo.[6,7] Every technique is allied with some pros and cons. However, nanocarriers are widely explored to enhance skin permeability owing to their favorable size that allow skin penetration without disrupting its functional integrity. Different types of nanocarriers are extensively utilized in designing TDDS. A variety of materials can be utilized for fabricating nanocarriers including metals, semiconductors, ceramics, lipids and polymers. Polymers are mostly explored for this purpose because of their in-vivo safety. On the basis of origin, there are two types of polymers i.e., natural and synthetic. Both categories of polymers find extensive application in nanomedicine and helping researchers to achieve unreachable therapeutic objectives.[8, 9]

Natural polymers including polysaccharides due to their intrinsic biomimetic biocompatibility serves as an ideal platform for safer in-vivo drug delivery.[10,11] In recent years, hydrogel nanoparticles fabricated by polysaccharides grab substantial attention of formulation scientist as a novel tool for nontoxic delivery of drug molecules through the skin.[12,13] Properties of both hydrogel and Nano architecture are amalgamate in these hydrogel nanoparticles. Among polysaccharides, chitosan (CHS) is cationic polysaccharide serve as a potential carrier for drug delivery due to their favorable intrinsic hydrogel forming properties. CHS can formulate nanoparticles by crosslinking with negative ion cross linker or polymer. Chondroitin sulfate (CS) is an anionic disaccharide ionically crosslink with CHS to form hydrogel nanoparticles. These CHS-CS based nanoparticles are emerging nanocarriers for the delivery of variety of therapeutic agents particularly in tissue engineering and repairing. Their natural innate properties that mimic extracellular matrix (ECM) make them ideal nanocarrier.[14-17] In this review role of chondroitin sulfate in designing nanocarriers for the transdermal delivery of NSAIDs to treat osteoarthritis is discussed in detail. This review also elaborates molecular mechanism of action of chondroitin sulfate and NSAIDs for the treatment of osteoarthritis.

Osteoarthritis

Arthritis is a chronic inflammatory disease associated with serious repercussion of severe joint pain, edema and disability. Almost 150 different types of arthritis have been documented on the basis of complexity of underlying inflammatory mechanism. However, osteoarthritis (OA) is the most prevailing form of disabling arthritis. In developed countries, OA ranked among ten most disabling diseases.[18] Inflammation in OA is allied with trauma or distress because of tissue injury that stimulate release of damaged associated molecular patterns (DAMP). DAMP elicit immune response by upregulating NF-kB (nuclear transcription factor kappa B) directly or indirectly. This upregulation leads to activation of variety

of chronic inflammatory mediators. DAMP comprised plasma protein damaged associated pattern, intracellular alarmins, crystals of calcium and cellular mediators.[19,20] Activation of these patterns result in production of proinflammatory mediators i.e., IL-1β (Interleukin 1β), MMP (matrix metalloproteases), TNFα (Tumor necrotic factor α). DAMP pattern also stimulates destruction of cartilage by chondrolysis which in turn enhance the release of plasma protein damaging patterns. Inflammatory mediator's proliferation results in increased vascular permeability and stimulates angiogenesis. This further exaggerates inflammation by producing plasma proteins that act as DAMPs. As a result of this inflammatory cascade migration of neutrophils and monocytes occurs by chemotaxis at injury site. These immune cells further worsen the inflammation by stimulation of mediators' reactive oxygen species (ROS), interleukins (ILs) prostaglandins (PGs) that stimulate edema at injury site.[21,22] All these mediators sensitize pain receptors that result in production of inflammatory symptoms i.e., redness, swelling in joints, temperature, loss of function and pain as depicted in figure 1.

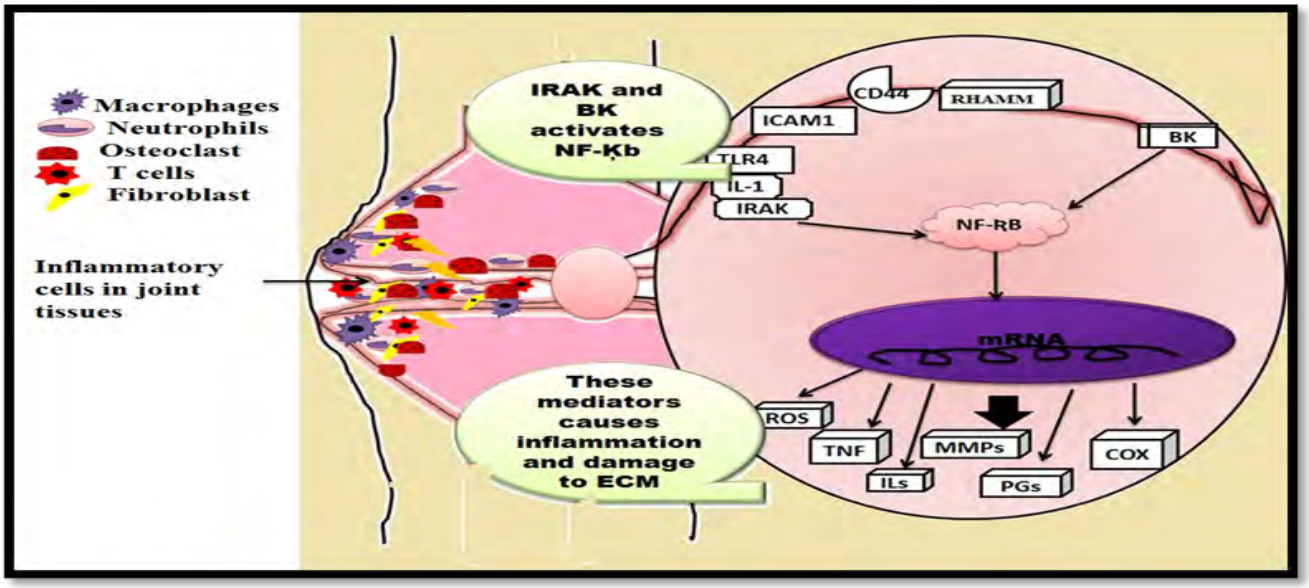

Figure 1: Inflammatory mediators in arthritis

[IRAK=Interleukin receptor associated kinase, BK=bradykinin, TLR4=Toll like receptor4, IL-1=interleukin-1, ICAM1=intracellular adhesion molecule1, CD44=Cell surface glycoprotein cluster differentiation44, RHAMM=Receptor for hylaronan mediated motility, NF-ķB= Nuclear transcription factor kappa B, ECM=extracellular matrix, ROS= reactive oxygen species, TNF= tumor necrosis factor, MMPs=matrix metalloproteases, PGs=prostaglandins, COX=cyclooxygenase].

Treatment of Osteoarthritis

Therapeutic objective of osteoarthritis treatment is to slow down the progression of inflammation and reduce pain. Current therapeutic regimen for the treatment of osteoarthritis comprised of NSAIDs,[23] Disease modifying anti-rheumatic drugs (DMARDs), glucocorticoids and biologics as key therapeutic agents.[24,25] Vivid progress in the development of innovative therapeutic agents that can effectively decrease the disease progression and slow down tissue damage thus improving quality of life of patient of this disabling disease. However, chronic nature of osteoarthritis requires long term application of drugs that leads to unwanted systemic adverse effects. NSAIDs are first line recommended therapy for symptomatic relief in acute and chronic stage. However, progressively damaging disease embroils use of DMARDs and biologics including immunosuppressant that are associated with severe life-threatening toxicities. As this chronic disabling disease prevails in old age patients who are less tolerant to these systemic toxicities. Localized delivery of drug by directly injecting drug into synovial fluid i.e. intra articular

injection may reduce side effects but frequent invasive injections also associated with patient compliance.

That's why today research goals prioritize development of targeted therapeutic strategies to alleviate systemic adverse consequences of non-targeted drug delivery [26] Conventional treatment of arthritis with associated adverse effects is described in table 1.

Table 1: Therapeutic regimen for osteoarthritis

Therapeutic class of drugs	Mechanism of action	Route	Systemic adverse effects	References
NSAIDs	COX inhibitors	Oral and parenteral	GI bleeding, ulcers, cardiovascular toxicity, renal toxicity	(22, 26)
Glucocorticoids	Phospholipase A2 inhibitors, Immunosuppressant	Oral and parenteral	Reduce calcium absorption. Osteoporosis, insulin resistance, obesity, CVS risk	(23, 27)
DMARDs	Cytotoxic and immunosuppressive	Oral and parenteral	Bone marrow suppression, hepatotoxic, nephrotoxic, cardio toxic	(23, 28)
Biologics	Monoclonal antibodies blocking receptors for inflammatory mediators	Parenteral	Reactions at injection site, neutropenia, fibrosis and increased chance of acquiring infections	(24, 29)

NSAIDs: Non-steroidal anti-inflammatory drugs
DMARDs: Disease modifying anti-rheumatic drugs.
COX: Cyclooxygenase

Role of NSAIDs in osteoarthritis

Non-steroidal anti-inflammatory drugs (NSAIDs) are first line cornerstone drugs prescribed for pain management in arthritis and osteoarthritis (OA). NSAIDs exert their therapeutic action by reversibly inhibiting cyclooxygenase (COX) that block the production of prostaglandins (PGs) from arachidonic acid (AA). Elevated level of PGs sensitizes peripheral nociceptors and exacerbate painful stimulus. In arthritis and OA, activation of signal transduction pathway promotes synthesis of proinflammatory mediators including COX and phospholipase A2 which ultimately produce more PGs in cartilage tissues and synovium that cause pain. This cascade of inflammatory process progress with disease that is responsible for chronic pain [22,31] NSAIDs chronic administration aid in reducing pain but prolong use allied with side effects of GI bleeding and ulceration.[32] Localized delivery of NSAIDs directly into joints by intra-articular injection reduces systemic effects but frequent injections for chronic use are not patient friendly and causes necrosis and pain at injection site. These side effects are eradicated by utilization of alternative route of drug administration i.e., transdermal route.

Transdermal drug delivery system

Transdermal drug delivery system emerges as an appealing substitute to minimize limitations allied with enteral and parenteral routes of drug administration. Drug delivery system that exploits the skin as an executable route for the purpose of producing systemic effects of drug is called transdermal drug delivery system. It includes application of drug to skin that is delivered to viable layer of epidermis and dermis which comprises capillary network from where it is absorbed and reaches systemic blood circulation. Transdermal differs from classical topical drug delivery system as later involves drug application for localized effect to skin for the treatment of skin diseases. This route is endorsed for the treatment of long-term chronic diseases such as pain management, arthritis, diabetes, cancer and hypertension due to sustain and control release of medicament over extended period of time. Feasible dose adjustment and monitoring, avoidance of first pass metabolism, reduction in side effects, zero order drug release and non-invasive

drug administration clearly depicts advantages of transdermal drug delivery system over other drug administration routes.[33]

Conventionally transdermal drug delivery system was designed in the form of adhesive patch. In 1979, US FDA approved first transdermal control release patch of scopolamine that results in opening of new gateway to transdermal drug designing for pharmaceutical design researchers. Today a number of transdermal patches have been approved for market use. Transdermal patches grab more than US $3 billion of annual US market. Despite the achievement of patch technology only a few numbers of drug candidates can be administered successfully through transdermal route due to constraining characteristics of human skin.[34]

The objective of drug delivery is to administer drug in a concentration that is safe to produce therapeutic effect to specific site of action for a particular time period. Transdermal route encompasses drug administration by way of the skin which is not only largest organ of human body but also perform protective function and control traffic of foreign materials and microbial population. This protective layer not merely impedes influx of foreign particles/toxins likewise serve as a barrier to drug delivery through skin that leads to reduced bioavailability of therapeutic agent. Only potent drugs with high lipophilicity and low molecular weight less than 500 Daltons could be administered through transdermal route. Therefore, a number of novel formulation designs and techniques have been employed to auspiciously subvert skin barriers. Advances in transdermal drug delivery system can be categorized into three successive generations as depicted in figure 2.

First generation comprises drugs having favorable characteristics for transdermal delivery. Second generation includes formulations to disorganize stratum corneum barrier by incorporating chemical penetration enhancers and physical permeability enhancing low voltage devices named as iontophoresis. Third generation of transdermal drug delivery encompasses physical and chemical techniques that reversibly disrupt or remove stratum corneum layer and bypass this permeability barrier to enhance delivery of macromolecules, proteins and vaccines.[35]

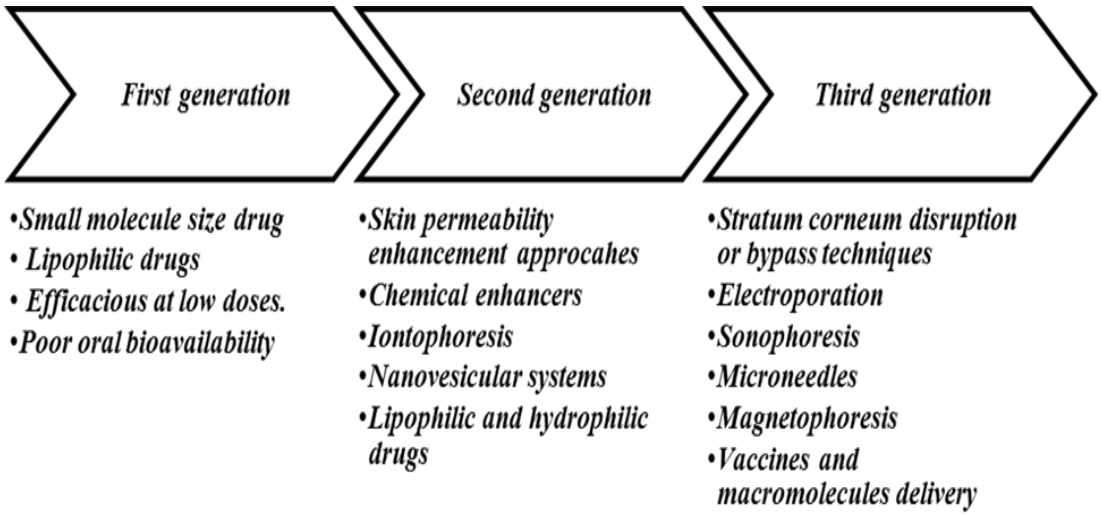

Figure 2: Advancement in development of TDDS Penetration pathways through the skin

There are two documented pathways for diffusion of substances through skin i.e., trans appendageal and trans epidermal conduit. Trans appendageal or trans follicular pathway composed of natural openings i.e., hair follicles; sebaceous glands, sweat glands so called shunt passage. This archway is area of interest for transdermal drug delivery designing researchers because of colossal network of capillaries adjoining pilosebaceous division. Meanwhile, mature SC is absent at the distal end resulting in entrance of drug candidate directly to contiguous tissues capillaries that successively deliver it to the systemic circulation. This passage is considered

suitable for delivery of hydrophilic drugs and macromolecules but foremost constrain in applicability of this passage is it comprises only 0.1% of total surface area of skin.

Other route is trans epidermal which is further assorted into two micro-conduits; transcellular (intracellular) and paracellular (intercellular) route. Intracellular route involves diffusion across SC composed of keratin protein so molecules diffuse through this protein layer and lamellar envelop however this route is not so important for transport of hydrophilic molecules because trans appendageal route is mostly utilized for this purpose. However, the important penetration enhancers enhanced transdermal penetration by reversibly altering secondary coiling of keratin proteins. Intercellular pathway is more preferred as this is continuous meander pathway between lipids domains. Lipophilic and amphiphilic molecules usually diffuse by this pathway. This pathway is composed of SC lipids in a specific hexagonal packing. Lipophilic molecules directly interact with these lipids and change their hexagonal packing. This alteration in lipids packing enhanced fluidity that allows drug penetration through the paracellular passage.[36, 37] Figure 3 portrayed skin anatomy and penetration pathways

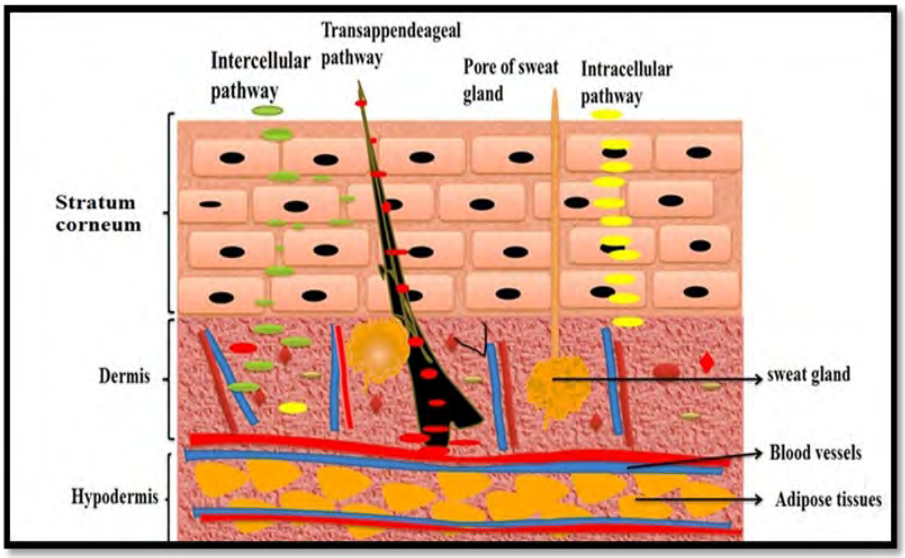

Figure 3: Drug penetration pathways through the skin nanocarriers for transdermal delivery of NSAIDs

Nanocarriers are extensively explored for their potential to overcome skin barrier and enhance penetration due to their size and surface properties. Therapeutic regimen of osteoarthritis requires long term drug administration with minimum adverse effects. To design drug delivery system for osteoarthritis, following important parameters must be considered. Primarily, drug delivery carrier provides sustain or control release of drug for longer period to avoid frequent administration. Then, carrier must be non-toxic and inert. Lastly, ideal carrier must deliver drug to specific inflammaed site to minimize systemic toxicities.[38] Therefore, NSAIDs therapeutic effectiveness can be enhanced by designing novel targeted drug delivery carriers that can alleviates associated systemic adverse effects.

Targeted drug delivery systems based on two basic strategies i.e., active targeting and passive targeting. Passive targeting entails advantage of pathophysiological condition of inflamed and tumorous tissue that is enhanced permeability and retention (EPR) effect due to leaky vasculature and angiogenesis. Carriers are specifically designed for passive targeting by controlling particle size, shape and nature. Active targeting implies utility of targeting ligands or homing devices that can specifically bind with intrinsic receptors at particular site of action. Targeting moieties includes peptides, polysaccharides, antibodies and nucleic acids. Nano-sized carriers made possible the utility of these targeting strategies.[39]

Polymeric nanoparticles are extensively employed for targeting in osteoarthritis as their surface can easily be modified with homing carriers for active targeting. Polymeric nanoparticles penetrate by way of skin appendages as well as transcellular and paracellular pathways depends on physicochemical properties, lipophilicity, molecular weight, surface charge and composition of polymer. Natural polymers possess intrinsic properties to mimic biological system and specifically interact with receptors so can be utilized for targeting therapy.[40] Hyaluronic acid (HA) specifically targets CD44 receptors overexpressed in synovial fluid utilized for delivery of salmon calcitonin. HA enhanced retention of calcitonin at inflamed joint and enhanced osteoprotective function as compared to free drug in animal models. [41] Chitosan also utilized for gene delivery in OA and results revealed chitosan as a successful gene vector for the delivery of IL-1Ra gene. Chitosan and chondroitin sulfate (CS) based hydrogel nanoparticles prepared by polyelectrolyte complex formation emerges as a suitable tool for pH based targeted drug delivery, transdermal drug delivery, protein drug delivery, tissue and cartilage regeneration. Chitosan-CS form polyelectrolyte complex (PEC) nanoparticles by electrostatic interaction between oppositely charged groups. Polysaccharides emulate the natural composition of ECM rendering them suitable drug delivery carriers in tissue and cartilage regeneration. Chitosan and CS based PEC membrane was designed for cartilage engineering and results depicted that this biomimetic membrane promotes chondrogenesis and tissue repair. Biomimetic microbeads composed of chitosan and CS based PEC film was utilized for delivery of mesenchymal stem cells (MSC).[42, 43]

This strategy promotes application of bioinspired polymers for fabrication of cell encapsulation system that cost effectively mimic natural cell environment of ECM for chondrogenesis and aid in healing process of damaged cartilage. These nanoparticles negate the need of surgical implantation into tissues owing to their enhanced penetration through membranes and cells thus improving patient compliance and safety. Meanwhile, hydrogel properties of nanoparticles provide sustain release of drug over long a period of time at desired physiological pH.

Role of Chondroitin sulfate in osteoarthritis

CS is a natural glucosaminoglycans (GAGs) with sulfate groups consist of N-acetylgalactosamine and glucuronic acid subunits. CS is present in connective tissues that is ECM of cartilage, skin, ligaments, blood vessels and tendons. CS is anionic disaccharide, attached with proteins in ECM forming key component of proteoglycans which is embedded in meshwork of collagen and elastin thus forming gel like consistency around cells. CS plays an important role in regulating cartilage function by stimulating synthesis of proteoglycan and type II collagen. Deficiency of CS results in osteochondral angiogenesis that leads to the progression of osteoarthritis. Thus, CS is approved nutraceutical agent for the treatment of osteoarthritis. NSAIDs when administered along with CS result in dose reduction of NSAIDs so is its associated side effects. CS plays its role to slow down the progression of osteoarthritis due to its intrinsic anti-inflammatory properties along with enhance synthesis of matrix protein of cartilage.[44]

CS display protective role in osteoarthritis and its detail mechanism of action is investigated to completely understand its potential. It has positive effect on articular chondrocytes, synovial membrane, and sub-chondral bone. CS play anti-inflammatory role by interaction with its receptors i.e., CD44, ICAM1, RHAMM and TLR-4. These receptors when activated results in reduction of signal transduction pathways for inflammatory mediators. Binding of CS with CD44 and ICAM1 stimulates production of IL-1 receptor associated kinases-M (IRAK-M) which inhibit IRAK that further slowdown the NF-kB nuclear translocation that ultimately reduced inflammation. IL-1 stimulates matrix metalloproteases expression i.e., MMP-3, MMP-9, MMP-13, COX-2, phospholipase A2. Inhibition of IL-1 indirectly result in reduction of all these inflammatory mediators that ultimately reduced inflammation in articular chondrocytes. CS also interacts with integrins which are responsible for enhanced expression of TGF-β1 that stimulates the production of collagen II and hyaluronic acid. Meanwhile, CS also reduced proteolytic breakdown of kininogen to bradykinin (BK) that also block signal transduction pathways as depicted in figure 4. Thus, by reducing inflammatory mediators and stimulating protective proteoglycans CS plays its chondroprotective function in

osteoarthritis.[45] CS due to its specific binding with receptors overexpressed in ECM during inflammation can also utilized as a homing device for designing active targeted drug delivery system in osteoarthritis. CS binds with CD44 receptors, annexin 6 and lectin receptors and transported inside the cell by receptor mediated endocytosis as shown in figure 4. Thus, CS can be utilized as a ligand for intracellular targeting. This innate property of CS makes this polymer as a promising biomaterial for designing of nanocarriers.

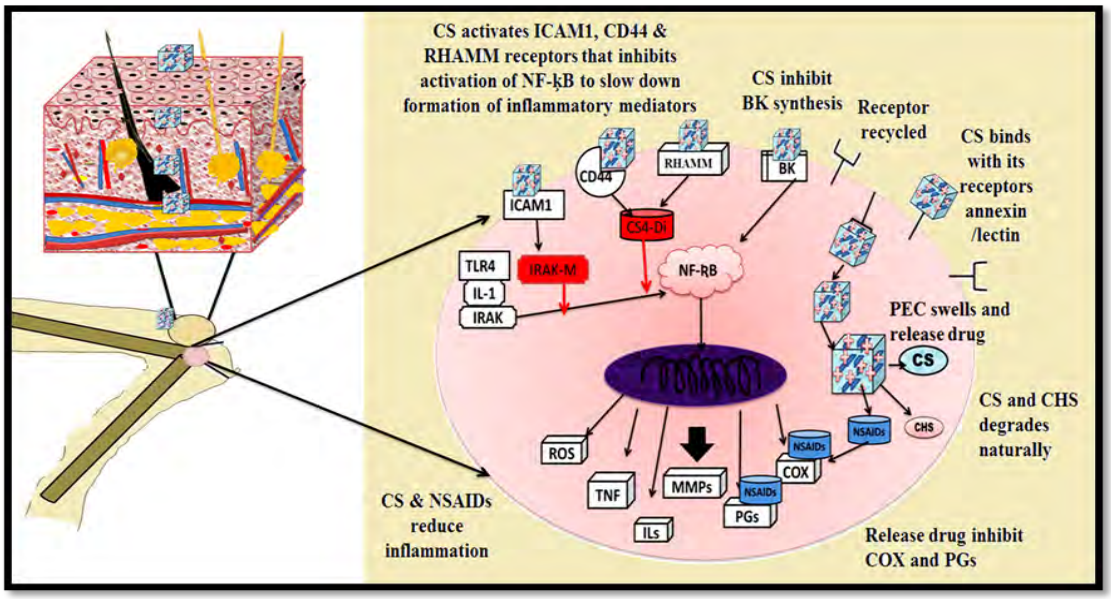

Figure 4: Mechanism of action of NSAIDs and CS

[ = Chitosan chondroitin sulphate PEC nps interacts with CS receptors and enter inside cell by receptor mediated endocytosis, IRAK=Interleukin receptor associated kinase,IRAK-M=inhihitor of IRAK,CS4-Di= monosulfated diasaccharide of chondroitin, BK=bradykinin, TLR4=Toll like receptor4, IL-1=interleukin1, ICAM1=intracellular adhesion molecule1, CD44=Cell surface glycoprotein cluster differentiation44, RHAMM=Receptorr for hylaronan mediated motility, NF-ķB= Nuclear transcription factor kappa B, ECM=extracellular matrix, ROS= reactive oxygen species, TNF= tumor necrosis factor, MMP=matrix metalloproteases, PGs=prostaglandins, COX=cyclooxygenase, NSAIDs=Nonsteroidal anti-inflammatory drugs, CS=chondroitin sulfate, CHS=chitosan].

CS can be attached on surface of variety of nanocarriers as a ligand. Surface functionalization of diacerein loaded solid lipid nanoparticles with CS deliver drug specifically to the inflammatory site in OA. Formulations with surface coating of CS showed higher accumulation in rat-inflamed joints as compared to formulation without CS. In another study, CS serves as homing device for delivery of aceclofenac loaded SLN and in vivo results revealed that CS functionalized SLN specifically accumulates in knee joints of rat.[42, 46] CS also finds utility for constructing polymer drug conjugates for targeted therapy. CS-glycyl-prednisolone drug conjugate showed better anti-inflammatory effect owing to enhanced retention at targeted site.[47]

CHS a linear cationic polysaccharide can form nanocarrier with CS by ionic crosslinking method. CHS also possess favorable intrinsic, biomimetic properties that enlighten its wide spread utility in drug delivery. [48] Chitosan can easily be formulated into hydrogels, membrane films, 3D scaffolds and nanoparticles for cartilage healing. Chitosan along with other GAGs serve as an ideal drug delivery carrier for tissue and cartilage repair owing to their innate properties of mimicking ECM structure and provide sustain release of drug at specific site. Biodegradability of these polymers further adds to their benefits as their degradable products are non-toxic and eliminate from body by natural catabolic processes. Chitosan being cationic polysaccharide ionically interact

with anionic polysaccharides that is CS to form polyelectrolyte nanocarrier. CHS-CS hydrogel mimic ECM and stimulate chondrogenesis. This hydrogel cultured on chondrocytes in laboratory showed chondrocytes retain their normal structure and function and promotes synthesis of collagen.[49] CHS-CS nanoparticles are also effectively utilized to deliver anti-arthritis drug through the transdermal drug delivery system.[42, 50] These intrinsic properties of biopolymers made possible to design the formulation with multiple functions i.e., targeting, therapeutic effect and enhanced skin permeability.

Conclusion

Engineering of novel biocompatible, biodegradable nanocarriers by utilizing natural sources is a promising strategy to achieve safer drug delivery systems. Biopolymers are ideal candidate for transdermal drug delivery system as these polymers improves skin permeability without producing any harmful effects on the skin. Chondroitin sulfate and chitosan not only enhance the skin permeability of the drug but also imparts synergistic effects in treatment of osteoarthritis by multi-dimensional targeting of the complex disease etiology. Chondroitin sulfate reduced the inflammation in osteoarthritis by down regulating number of inflammatory mediators by slow down the signal transduction of Nf-ǩB by binding with its specific receptors over expressed in inflammatory cells. These promising innate properties of natural polymers open a new gateway for researchers to design novel targeted synergistic drug delivery system with improved therapeutic outcome. However, a very few biodegradable and safer nanocarriers was explored for targeting in osteoarthritis. Thus, there is need of more research studies to investigate potential of biodegradable nanocarriers for targeted delivery of anti-arthritic drugs. To establish importance of natural carriers in drug designing, detailed understanding of carrier is very important. Furthermore, to achieve clinical outcome of experimental accomplishments more detailed in-vivo studies need to be addressed.

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CASE REPORT

Ischemic stroke is a rare finding in COVID-19 infected patients: A case report

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[2-5] Supervision

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A B S T R A C T

Coronavirus has become a global pandemic in short period and causing huge number of mortalities due to variety of complications caused by viral illness. Presentations from COVID-19 infection vary from mild respiratory symptoms, fever, pulmonary embolism, heart attacks and neurological manifestations to deadly acute respiratory distress syndrome. A case of elderly patient who was diagnosed as having COVID-19 infection with mild symptoms who was then admitted in hospital for the treatment of COVID-19 infection and then developed a massive ischemic stroke during the hospital stay. Coronavirus disease can present with atypical features for which clinicians should be aware of; so that the diagnosis and treatment should not be delayed and patient can receive maximum benefit with special emphasis on anticoagulant therapy in minimal symptomatic infection.

Keywords: *Coronavirus, ischemic stroke, hypercoagulable state, cytokine storm, Acute Respiratory Distress Syndrome (ARDS)*

Introduction

COVID-19 is a disease caused by novel coronavirus, also known as a severe acute respiratory syndrome coronavirus 2 (SARS-COV-2 virus) which had its origin from Wuhan city of china and now became a scary virus engulfing many precious lives worldwide. This viral illness has a range of symptoms varying from mild flu, fever and cough to acute respiratory distress syndrome (ARDS). Due to this virus, many valuable lives were snuffed out during this pandemic. Here a case of middle-aged male is presented who had COVID-19 infection and was admitted in hospital with his worsening symptoms but developed massive ischemic stroke during hospital stay.

Case report

A 59-years old male, previously known case of diabetes and hypertension for last two years with no established diabetic or hypertensive complications and well controlled with medications, presented in emergency department of hospital during COVID-19 pandemic with symptoms of fever, generalized body aches and loss of taste sensation for two days. Fever was high grade and associated with rigors and chills. It was continuous which relieved only with antipyretics. He was vitally stable with blood pressure of 125/79mmHg, pulse 82bpm regular, temperature 101F, and respiratory rate 16/minute and oxygen saturation 96% at room air. Chest examination revealed bilateral basal crackles. Other systemic examination was unremarkable. Due to history of positive close contact with COVID-19 patient, coronavirus disease was suspected and patient was admitted in isolation ward and all relevant tests send on urgent basis. Laboratory studies showed normal total leukocyte count with lymphopenia and raised levels of C-reactive proteins, D-Dimers, ferritin and interleukin-6.

Other investigations including liver function tests, renal function tests, and urine routine examination, blood and urine cultures were normal. Nasopharyngeal swab for COVID-19 Real Time PCR came out to be positive. Chest x-ray showing bilateral basal infiltrates pre-dominantly on peripheral margins of lung fields. High resolution computed tomography of chest (HRCT-chest) done which showed findings suggestive of COVID-19 pneumonitis. From the time of admission, patient was receiving antibiotics, antivirals, dexamethasone and enoxaparin in prophylactic dose. Patient remained vitally stable on first day of admission but developed sudden onset of right sided body weakness on seventeenth day of admission.

Patient's Glasgow coma scale (GCS) fell from 15/15 to 8/15, power 0/5 in right upper and lower limb, gag was not intact, with right sided up going planter. Patient was suspected to have associated cerebra-vascular accident. CT-scan brain was done within half hour of symptoms which has ruled out intracranial bleed.

So, the treatment of ischemic stroke was started. CT-scan brain was repeated after 2 days which showed massive left sided malignant middle cerebral artery infarct causing mild mid-line shift (Figure:1). Patient was managed according to left massive middle cerebral artery (including antiplatelet, mannitol and dexamethasone).

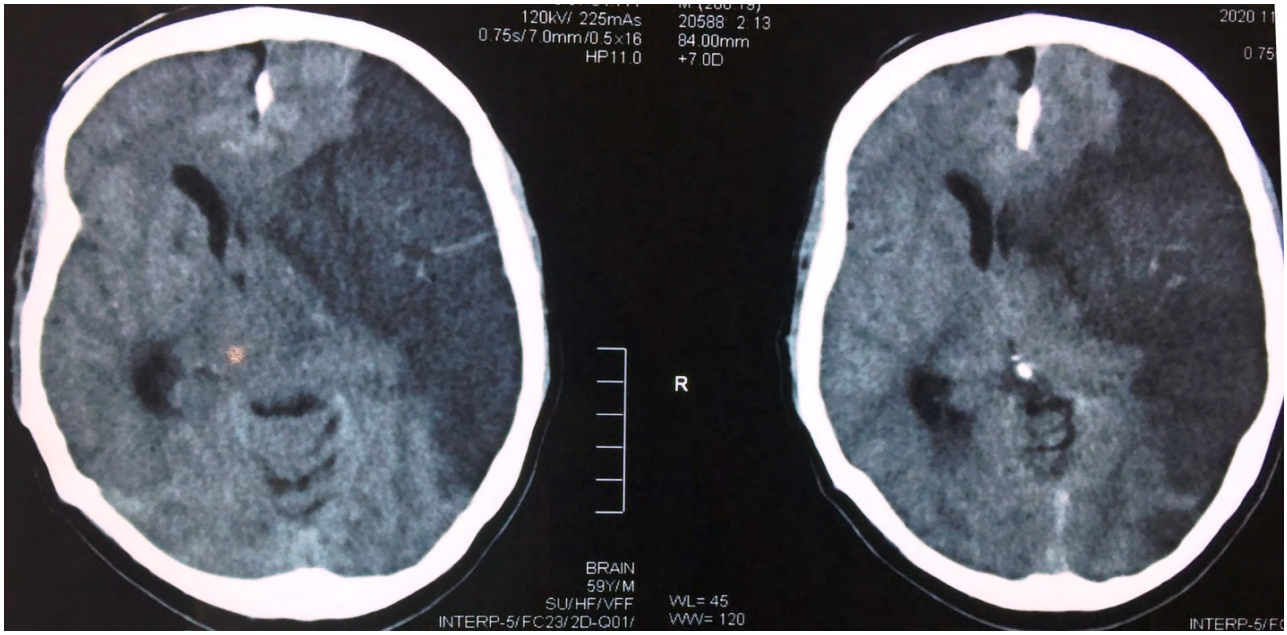

Figure 1: CT-Scan brain showing massive left frontal, parietal and occipital infarct.

Discussion

The patient was diagnosed as a case of massive malignant middle cerebral artery infarct which is a rare and atypical outcome of COVID-19 infection. He presented with typical feature of fever and shortness of breath but developed ischemic stroke on 17th day of symptoms onset. He was managed accordingly. Most of the cases published till date; patients usually have stroke on average of 12th day after symptoms onset but my patient had stroke on 17th day of symptoms initiation.[1] Novel respiratory virus, which was named later as severe acute respiratory syndrome coronavirus 2 (SARS-COV-2).[2]

Patients with COVID-19 infection usually present with flu, fever and respiratory symptoms but atypical presentations can also be present including symptoms from cardiovascular, central nervous system and gastro-intestinal systems.[2] There are broad clinical syndromes associated with COVID-19 infection which includes symptoms like dizziness, headache, anosmia, dysgeusia, peripheral neuropathy, altered mental status, acute psychosis, encephalitis, encephalopathy, neuro-cognitive (dementia-like syndrome), Guillain-Barre syndrome, acute kidney injury, myocarditis, acute respiratory distress

syndrome (ARDS) or stroke (ischemic or hemorrhagic).[1,3] Studies have shown more percentage of ischemic stroke rather than hemorrhagic one.[1] Acute ischemic stroke incidence is increased in COVID-19 infection compared with influenza.[4] It is also shown that patients with ischemic stroke associated with COVID-19 infection has increased incidence of death as compared to patients who did not developed ischemic stroke during COVID-19 infection.[4]

Medical personnel have noticed more severe ischemic stroke in COVID-19 infection. Reason for the ischemic stroke in COVID-19 infection can be inflammation, prothrombotic state, endothelial injury, cardiac abnormalities, underlying premorbid conditions, embolism, hypoxemia or infection.[2-5] Cytokine storm lead to vascular endothelial injury or a hypercoagulable state which may lead to micro vascular dysfunction and ultimately causing thrombosis.[6] This infection also causes venous and arterial thrombosis and is supported by increased D-Dimers, ST-segment elevation myocardial infarction (STEMI), deep venous thrombosis and pulmonary embolism in COVID patients.[6,7] Some authors have mentioned that patients who developed stroke due to COVID-19 infection usually had previous premorbid like hypertension or carotid stenosis and they observed to had stroke at average of 12 days after diagnosis.[3]

Performing the CT-Scan brain and diagnosis is often challenging as altered mental status, poor history and scarcity of visitors and caregivers and especially because of isolation protocols.[1, 2, 7]

Best medical care for acute ischemic stroke includes intravenous thrombolysis and thrombectomy; but simonescalard reported poor outcomes in patients treated with this therapy even after successful intervention.[8] The best treatment for acute ischemic stroke in COVID-19 infection has yet to be discover. Increasing prophylactic dose of anticoagulation to 40mg twice daily or higher is the treatment till now.

Conclusion

Increased number of strokes has been identified in patients with COVID-19 infection in this pandemic and causing intense strain and burn-out for health care workers and also on health care system.[5] Neurologists have to be prepared for increasing neurological cases during this horrifying pandemic.[4] Keeping in view this scenario, medical personnel have to be more vigilant about neurological deficits in COVID patients during or even after COVID-19 infection.

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LETTER TO EDITOR

Recommendations for management of burn patients in context of COVID-19 pandemic

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Author`s Contribution

[1] Wrote all parts of letter on the basis of experience of management of burn patients at Rawalian burn center RMU during COVID-19 pandemic

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Introduction

It has been reported from china that burn centers have the highest risk of COVID-19 infection.[1] The virus is highly contagious and damaging and mortality rate as high as 61.5% has been reported.[2,3] Burn patients have low level of immunity, lack skin barrier and are prone to infections. Due to these facts, they have less ability to fight against the corona virus, so surgical practices for management of burn patients should be modified to prevent the spread of infection and decrease mortality. Keeping these facts in mind, we adopted certain changes in the protocols for management of burn patients at Rawalian burn center, Rawalpindi Pakistan. We are presenting new recommendations which were followed at the burn center during COVID-19 pandemic. These are the first ever recommendations from any burn center of Pakistan since the start of recent pandemic. With help of literature search we identified risk factors for infection during the course of treatment of burn patients. These recommendations include alterations in structural layout, administration procedures, burn patient care like the introduction of telemedicine, online appointment system and use of online messaging applications i.e., WhatsApp, staff training and strategies like online learning system to provide new knowledge regarding COVID-19 continuously. Issues of staff like over work, availability of personal protective equipment (PPEs), and their health-related anxiety and fear should be addressed properly for the prevention of burn out syndrome in them.

Recommendations

Different studies from different parts of the world have put forward recommendations for management of burn patients in the context of the prevailing COVID-19 pandemic based on their local experience. Ning Li et al[4] in their recent study shared Chinese management strategies for burn patients during COVID-19 pandemic. They discussed their strategy regarding administrational, environmental, personal and surgical management. They also discussed the management of personal protective supplies and mental health of health professionals. Another Chinese study by Siyuan Ma[5] provided experience of managing burn patients and suggested changes required for burn treatment. The Spanish Association of Surgeons has put forward its recommendations for surgical management of patients infected by COVID-19 after conducting a detailed review of literature and internet search of websites WHO, CDC, ECDC and bibliographic search of published material regarding burn management.[6]

To apply these recommendations for burn management during COVID-19 pandemic, based on our local experience at Rawalian burn center RMU Pakistan, a special management plan was made. These recommendations are the first of their kind during this

recent pandemic. They are different from routine recommendations for burn treatment as certain COVID-19 related changes in structure of burn center layout and its administration procedures have been suggested in them. Following are our burn management recommendations in context of COVID-19 pandemic.

1. Changes in burn center administration system:

In Pakistan, tertiary care hospitals have emergency, inpatient and outpatient departments. "Rawalian burn center" receives its new cases mainly through the emergency department. In the context of the recent pandemic following changes are recommended in the administration system of a burn ward.

a) Formation of epidemic control team:

An epidemic control team should be made comprising of head of burn center, head nurse of the center, medical superintendent of the hospital or his representative, specialist from the pathology department and a member from infection control team of the hospital. A detailed policy according to WHO hospital emergency response checklist regarding epidemic control during all kinds of working in center should be developed and followed in true letter and spirit.[7]

b) Staff training:

All staff working in the center should be given training to deal with potentially infected patients. This training should comprise of two parts: Firstly, the knowledge about the disease should be provided by regular online classes and secondly the practical implication of this knowledge should be assessed to ensure that each staff member knows and applies it properly. Staff should know and practice the frequent hand washing and strictly wearing masks, goggles and face screens. This training can be done by watching videos and using internet and this should be a continuous and ongoing process.

2. Changes in burn ward layout:

Outpatient, Inpatient, emergency department and burn ICU as recommended by number of Chinese studies[8] should be divided into clean area, potentially contaminated and contaminated area and these areas should be clearly demarcated by the signs of different colors. New admissions should be kept in a separate area for 14 days and then shifted to the ordinary ward when they are clear. In this separate area, all standard operating procedures for handling COVID-19 positive patients should be followed. If the patient turns out to be COVID-19 positive then he/she should be shifted to the COVID-19 designated facility of the hospital for further management.

3. Disinfection policy:

Burn ward should be sterilized with the help of a circulating air sterilizer three times a day and each time this should be done for 30 minutes. Central air conditioning should not be done for the risk of spreading the infection. An infrared burn treatment apparatus is recommended for keeping burn patients warm. 1000mg/l Chlorine containing solution or 75% alcohol solution is recommended for disinfecting the surfaces. The floor should be disinfected with1000mg/l Chlorine containing solution by wiping or spraying method for at least 30 minutes. Air in public areas should be disinfected with acid peroxide and hydrogen per oxide by ultralow-capacity spray at least three times a day after evacuating the area.[9]

4. Admission policy:

The most important of all is the admission policy for new burn patients. Only those patients should be admitted to the burn center who cannot be managed away from the hospital where as patients with minor burns should be given first aid treatment and further management should be continued at home with online consultation from the burn center. Local health facilities can be of help in this regard also. Follow up patients should take consultations online by using internet or telemedicine and should only come to hospital when absolutely necessary. Those patients who need to come to hospital should get an appointment through online system so that the patients do not have to gather and wait unnecessarily in OPD.

5. Receiving new patient in emergency:

In the emergency department all new patients should be screened for COVID-19 in an area designated for this purpose preferably near the entrance of the emergency department. All staff working in the emergency department should follow standard guidelines for dealing

COVID-19 patients. If the patient turns out to be positive, then that patient should be shifted to COVID-19 management facility for further treatment by the multidisciplinary team of that hospital. Negative patients should receive the treatment according to the routine management plan but those patients who are admitted in the inpatient department should be kept in the quarantine area of burn ward for 14 days before moving to the general burn ward.

6. Guidelines for operative procedures on COVID-19 positive patients:

Following guidelines should be followed while operating upon COVID-19 positive burn patients.

a) After following all routine standard SOPs for surgical patients, informed consent should be taken in writing with a specific note that it cannot be signed because of the risk of spreading infection.
b) PPE Donning/Doffing sequence should be followed properly by the surgical team.
c) Checklists should be designed and used for all procedures on COVID-19 positive burn patients.
d) A separate operating room along with all required equipment should be designated for surgery of COVID-19 positive burn patients only away from the routine operation theatre complex.
e) A route for safe transfer of positive patients from the designated treatment facility to the operating room should be planned.[10]
f) Medical personnel traffic and their movements should be limited to minimal in the operating room to minimize the risk of contamination.
g) The number of health personnel involved in procedures that generate an aerosol should be kept to the minimum possible.
h) For incisions, electronic scalpel/cautery is recommended.
i) Instruments should be passed in a tray not by hand.
j) All unused drugs and disposable instruments should be discarded immediately after the procedure.
k) Operating room including all surfaces and anesthesia machine should be properly cleaned for a minimum of one hour between the procedures.
l) Hydrogen peroxide vaporization is recommended for decontamination of the operation theatre.
m) Elective surgery for the burn patients should be stopped during the pandemic.
n) Only the emergency surgery for burn patients should be done after screening tests like CBC and CT scan lung.
o) Health personnel involved in tracheal intubation and other procedures which generate an aerosol need to work with double preventive standards according to WHO guidelines.[11]
p) For procedures generating an aerosol, air isolation is recommended.

7. Management of traffic in and out of burn ward:

There should be separate entry and exit doors for staff, patients and their attendants in order to reduce overcrowding. Screening with a non-contact temperature measuring device like a laser thermal gun should be done at entry points. Frequent use of hand sanitizers should be done at entry points and in ward. All people entering the ward must be disinfected by antiseptic spray at the entry points. Only one attendant per patient should be allowed in the ward who must wear the mask and take standard protective measures. Doctors should try to maintain a distance of one meter from the attendants while talking to them. Suspected patients and attendants should be shifted to COVID-19 treatment facility of the hospital.

8. Protection of health personnel in burn ward:

As advised by specialized health care department of Punjab and other international institutions like china national protection plan[12] the layered method of protection must be used for health care personnel. Staff at places like outpatient department and burn ward should use primary protection where as for the staff at high risk areas (i.e. where there is direct contact with suspected and confirm COVID-19 cases), secondary and tertiary level protection should be used. Proper and effective use and availability of personal protective equipment (PPEs) must be ensured. Value of hand hygiene must be emphasized with the provision of proper knowledge and training to the staff.[8]

9. Recommendations regarding diet of burn patients:

Burn patients require high caloric protein diet for healing of their wounds, which becomes even more vital during COVID-19 pandemic. High protein diet with the addition of essential vitamins should be provided to burn patients and they should be encouraged to drink adequate water. Patients and their attendants should not be allowed to bring or order food from outside rather hospital cafeteria should be allowed to deliver food following the standard SOPs.

10. Dealing with psychological issues of burn patients:

As COVID-19 positive burn patients need to be isolated this may produce psychological disturbances like anxiety, loneliness, fear, and sleep disorders. So psychological assessment of these patients must be done to provide remedy for their issues. These patients also need more emotional support by the caring staff. Necessary and accurate information regarding their condition must be provided to them for their mental wellbeing to reduce their anxiety and stress. The same is true for quarantined health personnel, they should feel a sense of ownership by their institution. Their institution must remain in touch with them providing both medical and economic help thus reducing their stress and promoting mental health.

11. Preventing burnout syndrome in health personnel of burn center:

This is a very important issue in the context of the COVID-19 ongoing pandemic. Assessment for symptoms of burnout among health personnel should be done and appropriate measures should be taken to address the risk factors such as over work, fear and anxiety leading to its development.[13]

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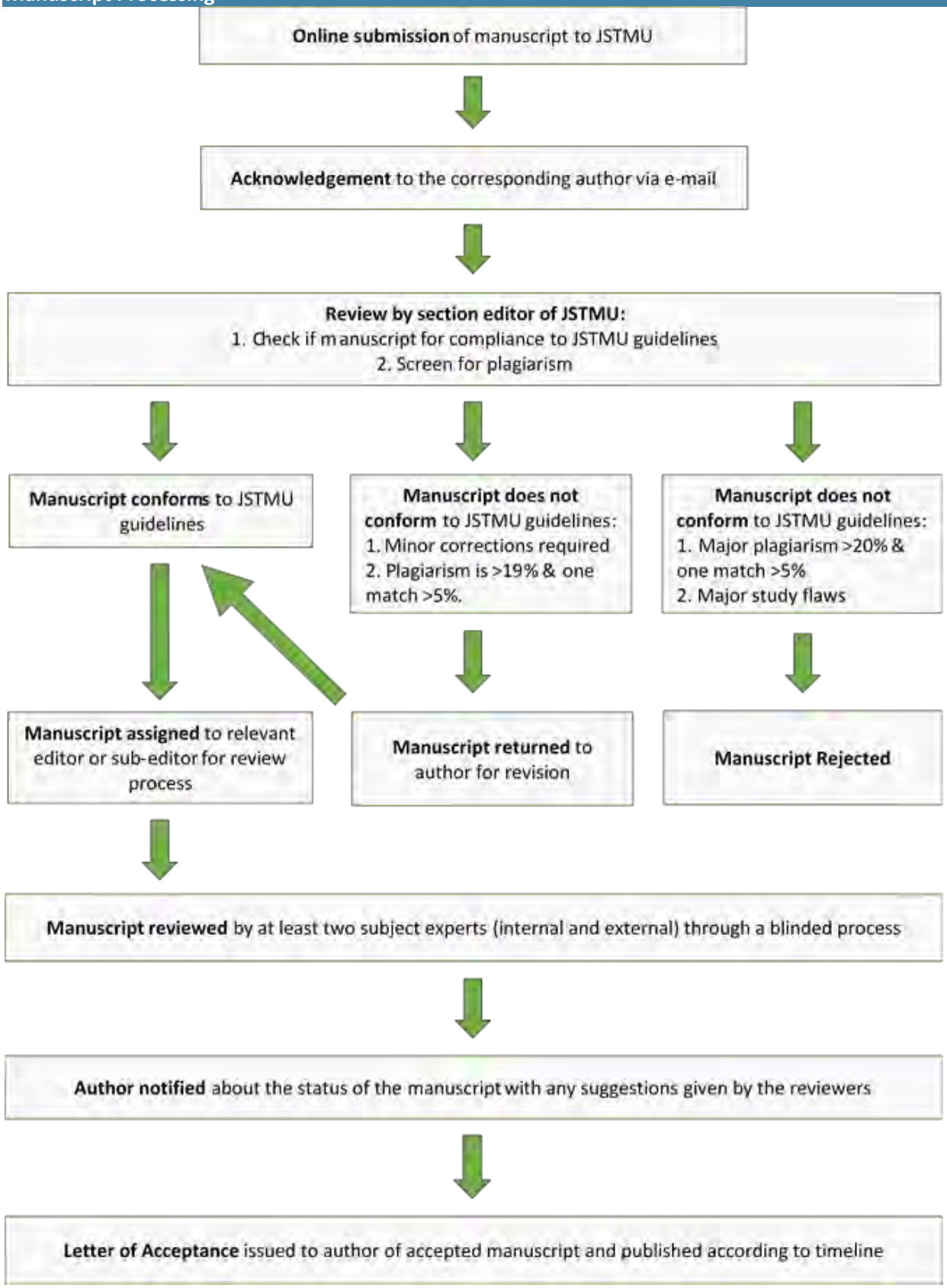

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A retraction note titled "Retraction: [article title]" signed by the authors and/or the Editor-in-Chief is published in the paginated part of a subsequent issue of the journal and listed in the contents list.

In the electronic version, a link is made to the original article. The online article is preceded by a screen containing the retraction note. It is to this screen that the link resolves; the reader can then proceed to the article itself. The original article is retained unchanged with a watermark on the PDF indicating on each page that it is "retracted."

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Abstracts and posters of conferences, results presented at meetings (for example, to inform investigators or participants about findings), results databases (data without interpretation, discussion, context or conclusions in the form of tables and text to describe data/information where this is not easily presented in tabular form) are not considered prior publication.

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The journal uses best practices for checking plagiarism in the content submitted and has the rights to inform the author and reject the manuscript based on set limits. Manuscripts are screened for plagiarism using iThenticate / Turnitin software. An unacceptable level of similarity will be returned for resubmission after appropriate corrections made by the author(s). Those found guilty or involved in publication misconduct are liable to be black listed.

Plagiarism is the unauthorized use or close imitation of the language and thoughts of another author and representing them as one's own original work. Within the academia, researcher is considered academic dishonesty or academic fraud and offenders are subject to academic censure. Plagiarism can be unintentional or intentional reproducing academic material without appropriate citation. Similarly, self-plagiarism is the re-use of significant, identical or near identical portions of one's own work without citing the original work. This is also known as "Recycling fraud". Worst form of plagiarism is to steal the whole article from some journal and publish it under own name in another journal. Lately the use of internet has made it easier to plagiarize, by copying the electronic tests and using them as original work.

The Editorial Board of JSTMU will **blacklist** any author found to be guilty of plagiarism. The name of author(s) committing plagiarism will also be disseminated to editors of other medical journals.

Types of Plagiarism:

We all know that scholarly manuscripts are written after thorough review of previously published articles. It is therefore not easy to draw a clear boundary between legitimate representation and plagiarism. However, the following important features can assist in identifying different kinds of plagiarized content. These are:

Reproduction of others words, sentences, ideas or findings as one's own without proper acknowledgement.

Text recycling, also known as self-plagiarism. It is an author's use of a previous publication in another paper without proper citation and acknowledgement of the original source.

Poor paraphrasing: Copying complete paragraphs and modifying a few words without changing the structure of original sentences or changing the sentence structure but not the words.

Verbatim copying of text without putting quotation marks and not acknowledging the work of the original author.

Properly citing a work but poorly paraphrasing the original text is considered as unintentional plagiarism. Similarly, manuscripts with language somewhere between paraphrasing and quoting are not acceptable. Authors should either paraphrase properly or quote and in both cases, cite the original source.

Higher similarity in the abstract, introduction, materials and methods, and discussion and conclusion sections indicates that the manuscript may contain plagiarized text. Authors can easily explain these parts of the manuscript in many ways. However, technical terms and sometimes standard procedures cannot be rephrased; therefore, Editors must review these sections carefully before making a decision.

Plagiarism in published manuscripts:

Published manuscripts which are found to contain plagiarized text are retracted from the journal's website after careful investigation and approval by the Editor-in-Chief of the journal. A 'Retraction Note' as well as a link to the original article is published on the electronic version of the plagiarized manuscript and an addendum with retraction notification in the particular journal.

Availability of data and materials

Submission of a manuscript to Journal of Shifa Tameer-e-Millat University implies that materials described in the manuscript, including all relevant raw data, will be freely available to any scientist wishing to use them for non-commercial purposes, without breaching participant confidentiality. JSTMU strongly encourages that all datasets on which the conclusions of the paper rely should be available to readers, and where there is a community established norm for data sharing, JSTMU mandates data deposition.

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Any questions raised during or after the peer review process will be referred to the Editor, who will request the original data from the author(s) for comparison with the prepared figures. If the original data cannot be produced, the manuscript may be rejected or, in the case of a published article, retracted. Any case in which the manipulation affects the interpretation of the data will result in rejection or retraction. Cases of suspected misconduct will be reported to the author'(s) institution(s).

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Authors should consider the following guidelines when preparing their manuscript:

Any statement in the manuscript that relies on external sources of information (i.e., not the authors own new ideas or findings or general knowledge) should use a citation.

Authors should avoid citing derivations of original work. For example, they should cite the original work rather than a review article that cites an original work.

Authors should ensure that their citations are accurate (i.e. they should ensure the citation supports the statement made in their manuscript and should not misrepresent another work by citing it if it does not support the point the authors wish to make).

Authors should not cite sources that they have not read.

Authors should not preferentially cite their own or their friend's, peer's, or institution's publications.

Authors should avoid citing work solely from one country.

Authors should not use an excessive number of citations to support one point.

Ideally, authors should cite sources that have undergone peer review where possible.

Authors should not cite advertisements or advertorial material.

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Editors will treat all manuscripts submitted to Journal of Shifa Tameer-e-Millat University in confidence. Our journal adheres to ICMJE Ethical Guidelines for peer reviewers. Reviewers are therefore required to respect the confidentiality of the peer review process and not reveal any details of a manuscript or its review, during or after the peer-review process, beyond the information released by the journal. If reviewers wish to involve a colleague in the review process, they should first obtain permission from the journal. The Editor should be informed of the names of any individuals who assisted in the review process when the report is returned. JSTMU will not share manuscripts with third parties except in cases of suspected misconduct.

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The Editorial team is responsible for the decision to reject or recommend the manuscript for publication. This decision will be sent to the author along with any recommendations made by the reviewers. After acceptance, it takes around 1-2 months to publish the article online, and a few weeks later this is compiled into an online volume and issue. The print copy follows within 3 months of acceptance of manuscript.

Initial decision to review	1-2 weeks after submission
Decision after review	6-8 weeks after submission
Anticipated timeframe for suggested revisions	3-4 months (with flexibility if needed)
Time to online publication	1-2 months after acceptance
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The manuscript(s) submitted to JSTMU should not be more than allowable words limit (mentioned in relevant sections below) and NOT more than 5 Tables and/or figures excluding abstract (250 words), acknowledgments and references. The text of the manuscript should be doubled spaced with one-inch margin on all sides. The font should be in size 12 Times New Roman and all pages should be numbered. A certificate, signed by the author and co-authors should be accompanied along with the manuscript stating that the article has been read and seen by all authors and have not been submitted or published in another journal or elsewhere in a report or textbook. Any copyright material, if used, should be accompanied with a permission letter from the copyright owner by the corresponding author. The manuscript should be checked for spelling and grammatical errors before submission. Authors should write the Keywords in the manuscript below the abstract. *

A. Original Research Articles

The Journal considers original articles that are, cohort study, case-control study, clinical trials, intervention study, epidemiological assessment, cross-sectional study, meta-analysis, cost-effective analysis, decision analysis, study of screening and diagnostic test, other observational studies, and qualitative studies such as focus group discussions, in-depth open-ended survey etc. Articles based on thesis maybe submitted provided the data is not more than three years old.

Each original article must contain:

Title page *

Title page should contain the following information:

1. Complete title of the article
2. Name(s) of author(s)
3. Department(s)
4. Institution(s) at which work was performed
5. Official phone/fax number, mobile phone number, personal e-mail address of the corresponding author, and institutions address.

Abstract

The abstract should be structured and NOT more than 250 words. The abstract must be written under the following subheadings:

1. Introduction
2. Objectives
3. Methodology
4. Results
5. Conclusion

Text

Text must be arranged under the following headings:

1. Introduction
2. Methods
3. Results
4. Discussion
5. Conclusion(s)
6. Acknowledgements (if any)

Introduction: Should provide brief review of relevant literature in such a way that it highlights the importance of the study and that the purpose of the study should be clearly stated. The articles used in the review of literature should be properly referenced by Vancouver Style.

Methods: Should include the setting(s), the subjects (participants), sampling methods and sample size, if used, type of study design used, and other procedures that were conducted. The Methods section should be brief, crisp and detailed enough to enable the reader to replicate the study in another setting. Commonly used procedures and methods need not be described but require a reference to the original source.

Results: Should include the factual findings of the research study done and, presented in the form tables or figures. Each table and figures should be properly labelled with headings and numbers (e.g. Table

No. 1, Figure No. 1) on separate pages. The write-up of results in the text should highlight the important findings without duplication of presentations displayed in the tables or figures. *Explanation of the findings should be reserved for the Discussion section.*

Discussion: Should highlight the important findings comparing and contrasting the study's results with that of other similar researches published and it should be appropriately referenced. Discussion should be concise and supported by the presented data.

Conclusion: Is restricted to the study and is drawn from the results and discussion.

Acknowledgements: If any, should be placed at the end of the text and before references.

References: *

References should be cited consecutively in SUPERSCRIPT as NUMERICAL without parentheses and should appear AFTER the punctuation marks (. , ; : ? ! " etc.) in the text/sentence. The final bibliography should be in the order in which they are quoted/cited in the text and written in *Vancouver Style*.

Citation Example:

Equal amounts of dietary carbohydrates have variable blood glucose response considerably as a function of specific food ingested.[1]

Bibliography/References Example:

1. Wolever TMS, Yang M, Zeng XY, Atkinson F, Brand-Miller JC. Food glycemic index, as given in Glycemic Index tables, is a significant determinant of glycemic responses elicited by composite breakfast meals. *Am J Clin Nutr* 2006; 83(6):1306–12.
   DOI: https://doi.org/10.1093/ajcn/83.6.1306

B. Meta -Analysis/ Systematic Reviews

Meta-analysis are systematic, critical assessments of literature and data sources pertaining to clinical topics, emphasizing factors such as cause, diagnosis, prognosis, therapy, or prevention, and that includes a statistical technique for quantitatively combining the results of multiple studies that measure the same outcome into a single pooled or summary estimate. All articles or data sources should be searched for and selected systematically for inclusion and critically evaluated, and the search and selection process should be described in the manuscript. Inclusion and exclusion criteria must be mentioned. Details of searching articles and search engines used should be clearly stated. The specific type of study or analysis, population, intervention, exposure, and tests or outcomes should be described for each article or data source. These should be described in the Method section. The data sources should be as current as possible, ideally with the search having been conducted within several months of manuscript submission. Authors of reports of meta-analyses of clinical trials should submit the PRISMA flow diagram and checklist. Authors of meta-analyses of observational studies should submit the MOOSE checklist. Follow EQUATOR Reporting Guidelines. The text **should NOT exceed 6000 words** excluding abstract, references, tables and figures.

Each of the sections of these articles should include specific sub-sections as follows:

Structured Abstract: (Not exceeding 250 words):

1. Objectives
2. Methodology
3. Results
4. Conclusion

Text should be organized under the following headings:

Introduction:

1. Rationale
2. Objectives
3. Research question

Methods:

1. Study design
2. Participants, interventions, comparators
3. Systematic review protocol
4. Search strategy
5. Data sources, studies sections and data extraction
6. Data analysis

Results:

1. Provide a flow diagram of the studies retrieved for the review
2. Study selection and characteristics
3. Synthesized findings

Discussion:

1. Summary of main findings
2. Risk of bias
3. Limitations
4. Conclusions

** For all other information including title page, typing and reference style, please follow the original articles instructions.*

C. Systematic Review (without meta-analysis): Review articles

Systematic Reviews/ review article are critical evaluation and assessments of scientific literature and other sources of data relating to health sciences topics, emphasizing factors such as cause, diagnosis, prognosis, therapy, or prevention. Systematic Reviews without meta-analysis are published as Review articles; those with meta-analysis are published as Original Investigations.

Systematic Reviews should include the following:

1. Abstract (Unstructured abstract of no more than 350 words)
2. Introduction (150-250 words)
3. Methods (150-250 words)
4. Results (1000-1250 words)
5. Discussion (1000 words)
6. Conclusions (2-3 sentences)

Maximum length: **Should NOT exceed 3500 words of text** (not including abstract, tables, figures, acknowledgments, references), with no more than a total of 5 tables and/or figures and no more than 50-75 references.

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D. Case Reports/Case Series

The journal will consider only those case report/series that represent very rare case(s), or epidemic diseases that are new or emerging, or first observation(s) of some emerging phenomenon or disease. They should have clinical significance and may also include observation of new adverse effect(s) of a drug, vaccine, or procedure or other unique observations, etc. Informed written consent of the patient or next of kin (if patient is not alive or comatose/disabled) should be obtained before submission of the manuscript. A covering letter from the authors that convincingly describe the merits of the case in the light of the mentioned criteria and it's educational or scientific merits should be sent along with the manuscript.

Case Report /case series should contain a single paragraph abstract and text **should NOT exceed 1000 words** (excluding abstract, references, tables and figures) with maximum 10 bibliographic references and either three figures or three tables. Each case report must contain:

1. Abstract (unstructured - should not exceed 120 words)
2. Introduction
3. Case Presentation
4. Discussion
5. Conclusion
6. Competing interest
7. Patient consent

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E. Rapid/Special /Short Communications

Rapid/Special/Short communication should be complete work, such as COMPLETE results of a short RESEARCH study, NOT a preliminary report and **should NOT exceed 1500 words** with one figure and/or one table. An editorial decision will be provided rapidly without reviews.

F. Letters to Editor

Letters should only be written on a specific article in the most recent publication of journal. The letter should be objective and provide constructive opinions offer some academic or clinical interest to the readers.
Letters **should NOT exceed 400 words** of text and 5 references, 1 of which should be to the recent article. It should not have more than 3 authors. The text should include the full name, academic degrees, and institutional affiliation for author and the email address for the corresponding author. Letters considered for publication shall be forwarded to the author of the cited article for possible response. The editor reserves the right to shorten these letters, delete objectionable comments, make other changes, or take any other suitable decision to comply with the style and policies of the journal. For writing and references style, follow the same instructions listed above.

Letter in Reply

Replies by authors should not exceed 500 words of text and 6 references. They should have no more than 3 authors.

G. Editorial

The topics of the editorial are decided by editorial board and/or Editor-in-Chief. Editorial is written either by one member of the editorial board or some expert on that topic invited by the Editor-in-Chief. As a convention, the editorial addresses relevant areas of interest that may pertain to a range of areas influencing health and health care sciences.

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