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Oasis of knowledge

The hand drawn illustration on the cover of JSTMU encapsulates philosophy of the University and its Journal. It depicts a traveler in the desert stopping by an oasis to take a note to themselves, symbolizing the point after which their journey requires steadfastness and dedication. The note is an excerpt from the Qur'an where God beseeches human beings to reflect. This is the essence of scientific research which prescribes itself in the University logo and is represented through red and blue color in the form of the water and the red sand, and taking further inspiration in the form of the notebook and the quill.

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EDITORIAL

A dire need for recruitment of rehabilitation professionals for provision of geriatric care

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Keywords: *Geriatric care, quality of life, rehabilitation, recruitment*

The rapid surge in Pakistan's population is exacerbating the demand for rehabilitation professionals with attributable factors such as an aging population, rise in chronic and complex multi- system disorders, improved evaluation methods for disability,[1] advances in technology, and changes in inter-professional health service delivery models. However, health human resource (HHR) strategies for rehabilitation professionals are lagging behind in comparison to other professional groups such as physicians and nurses. A field of healthcare which has suffered from neglect or to put it in another manner is largely ignored is geriatric care.[2] In Pakistan the number of medical healthcare professionals is insignificant. Whether this is on account of adopting a traditional treatment plan, subscribing to palliative care, being resigned to one's fate or simply ignorance of geriatric care being an emerging discipline is debatable. What is understood that as a discipline it does not exist prominently with two major fallouts. The first being that the socio-economic burden on the caregiver increases and second fallout being the geriatric patient ceases to be a productive individual of the society thereby the load on the healthcare system rises. To analyze this existing scenario, it is imperative that a study be conducted to identify recruitment strategies of rehabilitation professionals including medical professionals, occupational therapists, speech language pathologists and physical therapists to determine and investigate the importance, selection and identification of strategies using expert panels amongst HHR, public healthcare and academia, these being essentially required for rehabilitation services.[3] Further such an academic endeavor can invoke debate, inspire research and recognition of the enabling articles/ provisions for health care guaranteed in the Constitution of Pakistan by the state to its citizens specifically the vulnerable population.[4] The geriatric population of any developing country like Pakistan, with a fragile healthcare structure, has a vulnerable geriatric population as highlighted by the World Health Organization (WHO) wherein a high prevalence of disability of 15% has been reported by WHO,1 with 31 million disabled in Pakistan.[5] Disability in the geriatric population is increasing due to increase in chronic illnesses as well as the ageing population.

Geriatric rehabilitation services are part and parcel of a health system and handle persons with disabilities through an integrated multidisciplinary strategy in most effective programs and includes thorough assessment strategies and intensive rehab which is evidence based and patient targeted.[6] This invariably commences with a physician prescribing a rehabilitation plan, be it disability arising out of diseases or trauma and involving Rehab nurse, Speech language pathologists, Physical therapist, Occupational therapist, Audiologist, Prosthetists and orthotists, social case workers, as well as Psychologists. Unfortunately, in Pakistan shortages of rehabilitation manpower are arising being a lower income country and the geriatric population being marginalized despite its size increasing, this is also aggravated by dearth of training in geriatrics & gerontology.[7]

In Pakistan geriatric rehabilitation can be classified as a comparatively new profession with physical therapy

diploma courses starting in1956, now being offered by 69 institutes, and PhD in Rehabilitation sciences being offered in barely a few universities.[8] Rehabilitation services in Pakistan till 2011 were marred with just a few rehabilitation departments suffering from an inherent lack of integrity of rehabilitation team, with only 38 Rehab consultants and 1000 physical and 150 occupational therapists,[9] although the situation has marginally improved currently. Despite being the 3rd largest healthcare workforce, shortage of rehabilitation professionals including occupational therapists and speech language pathologists still haunts this critical field of healthcare as recruiting and retaining rehabilitation workforce is yet another challenge.[10]

The situation is not so simple that merely demand and supply would influence both recruiting and retaining decisions of rehabilitation professionals in tertiary care hospitals as healthcare professionals are only of late in Pakistan inclined to advocate geriatric care. Academia and hospital administrators need to focus as well as to minutely study geriatric health issues in the perspective of patients' rights as the self-esteem and physical, psychological and social aspects of quality of life of this vulnerable strata is being compromised,[11] accentuated by the fact that they traditionally and culturally assert their productivity and non-dependency potential. As productivity of the elderly and aged population is compromised their earning capacity and self-esteem suffers as well. The scope of any study may incorporate making sources of data available for structural improvements, guarantee the overall study of whole rehab manpower irrespective of individual specialty, to staff less served areas for increasing education, attraction and tele-health, to promote different policies in settings of rural or urban and to replicate international evidence based best practices.

It goes without saying that in developing countries like Pakistan, rehabilitation services require further integration in hospital healthcare system along with stressing upon educational needs and ethical and professional development to produce and later recruit rehabilitation professionals. With stigmas and cultural norms hindering tucking-in the disabled into the society,9 it can be safely concluded that there is a myth prevalent amongst the public health profession at large that the healthcare structure of Pakistan cannot cater to the geriatric population which is most vulnerable including the disabled. Compromise on public health amounts to compromise on a country's development agenda and is the worst form of intellectual dishonesty.

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EDITORIAL

Current landscape of pharmacovigilance in Pakistan

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Keywords: *ADR Reporting, DRAP, medication safety, patient safety, pharmacovigilance*

Pharmacovigilance is the process of evaluation of a new drug molecule for any adverse drug reaction before it is marketed. The history of pharmacovigilance is an old one and dates back to half a century ago. The concept gained momentum after the thalidomide tragedy.[1] it undergoes a lot of studies to make sure that it is safe for human use. During clinical trials, the potential benefits as well as risks of a certain drug molecule are evaluated. This is done in order to introduce a safe and effective drug to the patients. It is important to mention here that the process of pharmacovigilance spans the pre-marketing as well as the post-marketing surveillance. During clinical trials, it is necessary to remain vigilant and document any adverse effects experienced by the subjects enrolled in the trial. After a therapeutic good has been introduced in the market, spontaneous reporting is practiced to scrutinize any life threatening effects. These side effects may be dose dependent or dose-independent and this is the point where consumer reports play an important role.[2] Eradicating any such effects would guarantee patient compliance to the therapy and desired therapeutic outcomes.

In Pakistan, the concept of pharmacovigilance arose after numerous deaths were reported due to administration of counterfeit Tyno cough syrup and adulterated Isotab tablets.[3] These two incidents prove to be monumental and paved way for establishment of Drug Regulatory Authority of Pakistan in 2012 followed by establishment of multiple Drugs Testing Laboratories (DTLs) all over Pakistan. The main objective of these institutions was to standardize the quality of medicines produced within the country and to ensure safe medication therapy for the citizens. In order to play its role in international healthcare community, Pakistan became 134th full member of the WHO Programme for International Drug Monitoring (PIDM) in 2018.[4] Currently, Pakistan National Pharmacovigilance Centre (PNPC) has been designated by DRAP as the national center for reporting Adverse Drug Reactions (ADRs) that collaborates with Uppsala Monitoring Centre (UMC) and analyses ADR reports received from. Provincial Pharmacovigilance Centers (PPC). Special instructions have been issued to regulate the usage of High Alert Medications and Look-Alike & Sound Alike drugs (LASA) medicines.

The role of Primary and Secondary Healthcare Department, Government of Punjab with regard to enabling pharmacovigilance activity in the province is applaud able. The department has designated Pharmacovigilance Officers in all health facilities under its administrative control who are responsible for on-spot detection and reporting of any ADR that may occur. A dedicated portal, Medicine Surveillance System (MSS), has been designed for reporting purpose.[5] It allows the pharmacovigilance officers to report any Therapeutic Goods Related Problem (TGRP).

The scope of pharmacovigilance is vast and it encompasses any adverse drug reactions, adverse drug events, adverse effects following immunization (AEFIs), quality and efficacy issues associated with therapeutic goods and any side effects resulting from misuse, abuse or off-label use of therapeutic goods. As the DRAP Act 2012 regulates the production and use of biologicals, alternative medicine, nutraceuticals, cosmeceuticals along with allopathic medicine, any problems associated with any of these products is reported to pharmacovigilance centers. Here it would be crucial to mention that both PNPC and PPC have designated ADR reporting forms or drug & device complaint (DDC) forms available at respective official websites which can be filled in by the healthcare

professionals or the patients who encountered any ADR and sent to regional pharmacovigilance center. Recently, DRAP also launched a MedSafety mobile app that can be downloaded from App Store and Google Play and allows the user to report any ADRs from their cell phones.

In order to establish a stronger ADR reporting environment, following measures need to be taken.

1. Structured training sessions complying with international standards for focal persons.
2. Establishment of Drug Information Centres (DICs) and Poison Control Centres (PCCs) in all hospitals.
3. Encouraging the physicians, pharmacists, nursing staff & allied healthcare workers to report ADRs.
4. Awareness sessions for public regarding ADR reporting and its benefits.
5. Public awareness campaigns for using ADR reporting forms and MedSafety app.
6. Easily accessible ADR reporting means for the public like the Yellow Card Scheme in UK.
7. Teaching pharmacovigilance to doctors, pharmacists, nurses and allied healthcare providers as part of curriculum.
8. Formulation of National Pharmacovigilance Policy.
9. Allocation of funds for pharmacovigilance activities in Research & Development sector in research institutes and industry.
10. Development of informatics tools including trigger tools with user friendly interface to detect and report ADRs.

The future of pharmacovigilance in Pakistan is seemingly bright as efforts are being made on governmental level to establish an environment that encourages the healthcare professionals to report any unwanted effects experienced by end users of therapeutic goods. It is hoped that soon a successful pharmacovigilance system would be set up all across the country to ensure medication and patient safety.

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ORIGINAL ARTICLE

Critical thinking dispositions' level among neophyte nursing students

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[1,2] Conceptualization, data collection, analysis, Interpretation and Article writing

[3-4] Data analysis, review, article writing

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A B S T R A C T

Introduction: Critical thinking dispositions (CTD) are valued across the health professions disciplines being essential for decision-making, critical judgment and managing complex health situations. Promoting critical-thinking dispositions in undergraduate nursing students can support the students to utilize critical thinking during challenging patient care and problem-solving situations.

Objective: This study aimed to assess the level of critical thinking disposition among neophyte nursing students in a private nursing college, Islamabad.

Methodology: An analytical cross-sectional study design was adopted. Neophyte students (n=98) of the BSN program participated in the study. Critical Thinking Dispositions Scale (CTDS) of 54 items under seven constructs (Contextual perspective, Perseverance, Reflection, Intellectual integrity/ truth – seeking, Creativity, Open-mindedness and Inquisitiveness) was utilized to assess CTD level. Data was analyzed at descriptive and inferential level using SPSS 23.0 version.

Results: Overall, CTD among neophytes nursing students is at 75% a progressive level. Contextual and inquisitiveness construct of CTDs are at positive CTD level while other constructs are at the progressive level. Students have completed their matriculation from public 55(56.1%) while FSc (Faculty of Science) from private sector 57(58.2%). Mothers of most neophytes 73(74.5%) were housewives and fathers were working in private organization 32(32.7%). There was no statistically significant association between CTD's construct with demographic variables (P-Value, >0.05). FSc marks showed a significant association with overall CTD scores, intellectual and inquisitiveness, while admission entry test scores associate significantly with intellectual construct.

Conclusion: The CTD level of neophyte is at a progressive level which suggest that different teaching and learning strategies could be implemented to improve this level.

Keywords: *Critical thinking, critical thinking disposition, critical thinking dispositions scale, neophyte*

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Introduction

Critical thinking disposition (CTD) is essential for decision-making, critical judgment and managing complex health situations therefore valued across the health profession disciplines. Due to dynamic nature of the clinical environment, nurses should be prepared to be competent, safe and confident, which is possible if CTD is the emphasis in the clinical practice.[1]

The roots of CTD emerge from critical thinking (CT) which is a multidimensional concept and has multiplicity in it that can be viewed in terms of skills, applicability and

accomplishment.[2] Moreover, critical thinking is active and organized intellectual process focusing one's own thinking and keeping others thinking away. Critical thinking is constituted through both dispositions and CT Skills, CT skills developed through the instructions and the dispositions are "habits of mind" so its development requires long-term participation in learning environment.[3] Critical thinking is constructive in evaluating complex situations and implementing appropriate actions and requisite for problem solving and decision-making. Therefore, among the health care professional critical-thinking is more important, because they are directly involved in patient care like nurses, doctors, and physiotherapist.[4] When not enough evidences are available to support practice, nurses need to utilize critical-thinking to deal with practical situations. Hence, critical thinking disposition is essential in health care for decision-making, critical-judgment and managing of complex situations.[2]

Critical-thinking is the foundation of nursing practice and is crucial in the current complex situation.[5] A study conducted in Turkey reported freshmen students mean score 220.07± 17.7 in nursing college.[6] Another study reported the average critical thinking disposition score 194.48±14.20 at the start of the program.[1] Therefore, many health professions, including nurses promote critical thinking. Furthermore, promoting critical-thinking dispositions in undergraduate nursing students can support the students to utilize critical thinking during challenging patient care and problem-solving situations.[7]

In Pakistan, the focus of nursing education is generally rote-learning rather than utilizing critical thinking.[4] Consequently, CTDs are not well developed among Pakistani nursing students. Notwithstanding the dearth of research in Asia on this phenomenon, there is also no evident research in Pakistan regarding assessing critical thinking disposition among neophyte nursing students. It therefore became imperative to conduct research in a Pakistani context, assessing the level of critical thinking dispositions in neophyte nursing students, to utilize the outcome for addressing the CTD-deficiency.

Purpose of the study

The purpose of this study was to assess the levels and association of critical thinking dispositions among neophyte nursing students in a private nursing college, Islamabad.

Research questions

1. What is the critical thinking disposition among neophyte nursing students at a private nursing college?
2. What is the association between critical thinking disposition and demographic variables among neophyte nursing students at a private nursing college?

Methodology

A quantitative research approach was adopted to conduct this research.[8] Analytical cross-sectional study design was used for this study.[9] The study was conducted at a Private College of Nursing, Islamabad during March to September 2020. The study population included neophyte students of the Bachelor of Science in nursing (BSN) program; this refers to year-1 students who were enrolled in the BSN Program. Universal sampling technique was employed in the current study.[10] Thus, finally 98 participants were recruited. All the students enrolled in the first semester of BSN program were invited to participate in the study.

Instrument

First section of the tool included demographic characteristics of the study namely gender, age, educational status and parent occupation of the student. Cordially, section two contained critical thinking dispositions; permission to use the tool was taken. Importantly, to minimize the barrier in assessment, CTDs scale is developed in Pakistani context; it is available in English as well as Urdu languages. This CTDs scale is beneficial because it can provide better understanding of the items in local context. The CTDs scale comprised of 54-items under seven constructs including contextual perspective (5-items) denotes taking into account the complete picture of the situation in hand and its actual circumstances prior to making any decision; perseverance (7-items) means an individual's level of self-control and willpower to remain persistent, determined and firm to serve the purpose; reflection (7-items) is an individual's' insight awareness to evaluate, critique and correct own behaviors and actions; intellectual integrity/ truth-seeking (9-items) is an ability to be consistent being logical, rational, straight forward, moral, truthful, self-disciplined,

and reliable while dealing with others and/or any situation; creativity (7-items) is an individuals' talent to do new things and thinking of innovative ideas; open-mindedness (10-items) means aptitude to give space to accept others' point of view and customs; and inquisitiveness (9-items) is considered as the eagerness to explore the depth and breadth of the hidden knowledge to comprehend the truth.[11] Responses of the items were measured on 5-point Likert scale from 1-5 (1-strongly disagree, 2-disagree, 3-somewhat agree, 4-agree, 5-strongly agree). From the 54-items, 42-items were positive and 12-items were negative. The negative items were marked inversely on the scale 1-5 (1-strongly agree, 2-agree, 3-somewhat agree, 4-disagree, 5-strongly disagree).

The CTD scale scores were divided in three levels: Positive, progressive and negative. Following were the category of level of Critical Thinking Disposition Scale (CTDS) used to calculate CTD cut off score in Table 1.

Table 1: Criteria of CTD Categories

Sr.	Level of CTD	Cut- off score	Percentage
1	Positive CTD level	216 – 270	80 – 100%
2	Progressive CTD Level	135 – 216	50 – 79.99%
3	Negative CTD Level	<135	<50%

The sub scales scores range from minimum to maximum: Contextual Perspective (5–25), Perseverance (7-35), Reflection (7-35), Intellectual integrity/ truth - seeking (9-45), Creativity (7-35), Open-mindedness (10-50) and Inquisitiveness (9-45). Each subscale cut off score was: 80-100% positive CTD level, 50-79.99% progressive CTD Level and less than 50% negative CTD Level.

Pilot Testing

Pilot-testing was conducted on 10% of the sample size that is nine students. The average time to complete the questionnaire was 20-minutes. Since the tool was in English and Urdu (national language) there was no linguistic or other problem identified in the pilot study. The Cronbach's alpha was measured at 0.847 which is favourable.[12]

Data collection

Data collection process was initiated after the approval of Institutional Review Board and Ethics Committee. Approval from institutional head was also taken. In order to maintain the principle of anonymity, a program secretary, who was trained for the data collection approached students after their class schedule to explain them about the purpose and other aspects of research concerning informed consent. Students were informed that their participation was voluntarily and have the right to withdraw from the study without giving a reason. Data collector generated the serial code and the primary researcher was kept blind regarding students' identity. Students were provided with the participants information sheet, consent form and data collection tool. Students were requested to return the forms after two days. Lastly, the data collector handed the data to primary researcher for the analysis.

Statistics

Data was analyzed using Statistical Package for Social Sciences SPSS (Version 23.0). Data was entered and assessed for inconsistencies. Descriptive statistics like mean, standard deviation were applied and frequency was calculated for demographic and CTD variables wherever applicable. Inferential statistics like chi-square or Fisher exact test was applied to measure the association between demographic variables and CTD variables.

Results

Data was thus collected from (n=98) participants, who were neophyte (se mester-1) BSN nursing students. Majority of the participants (50) had age between 15-20 years. Most were females (68.4%). Concerning educational background, 55 students completed their matriculation from the public and 57 completed their FSc from the private school system. Regarding occupation status 3/4th of the students' mothers were housewives and 32 of the fathers worked in private organizations. The average FSc marks of students were 67.6 ±9.9 whereas the entry test score was 70.7 ±5.4. Further details of demographic variables are presented in Table 2.

Table 2: Demographics

Variables		Frequency (%)
Age	15–20 years	50 (51.0)
	21–25 years	48 (49.0)
Gender	Male	31 (31.6)
	Female	67 (68.4)
Matric	Public	55 (56.1)
	Private	43 (43.9)
FSc	Public	41 (41.8)
	Private	57 (58.2)
Mother's occupation	Housewife	73 (74.5)
	Nurse	10 (10.2)
	Teacher	11 (11.2)
	Other	4 (4.1)
Father's occupation	Government	14 (14.3)
	Private	32 (32.7)
	Labourer	22 (22.5)
	Business	22 (22.5)
	Not working	8 (8.2)

The overall average critical thinking dispositions score was at 75%. Majority of the students had CTD at a progressive level. Out of seven constructs three constructs do not have negative level of CTD. Contextual (68) and inquisitiveness (64) constructs score revealed that participants had positive CTD. Highest numbers of students (91) were in progressive construct of open-mindedness. Furthermore, the average score of CTD constructs was between 20.4 to 37.0 with variation ranged ±1.8 to ±3.7. For detailed information of critical thinking disposition and its constructs refer to figure 1, table 3.

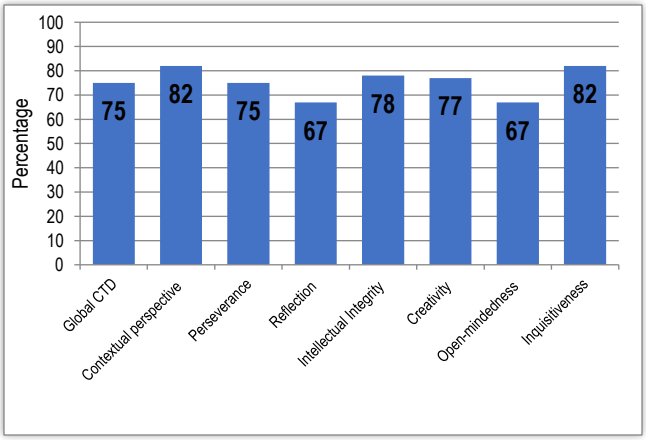

Figure 1: Percentages (levels) for global and constructs of CTD.

CTD constructs and demographic variables

Overall, there was no statistically significant difference of CTDs constructs among the demographic variables (P-Value, <0.05). In addition, all the subscales/constructs of CTDs were positive. The age was strongly associated with contextual CTD.

Table 3: CTD Score and its Constructs

Constructs of Critical Thinking Dispositions	Contextual CTD Levels		
	Negative	Progressive	Positive
	(≤49.99%)	(50-79.99%)	(80-100%)
	f(%)	f(%)	f(%)
Overall CTD	-	83 (84.7)	15 (15.3)
Contextual	-	30 (30.6)	68 (69.4)
Perseverance	-	60 (61.2)	38 (38.8)
Reflection	3 (3.1)	80 (81.6)	15 (15.3)
Intellectual Integrity	1 (1.0)	51 (52.0)	47 (48.0)
Creativity	1 (1.0)	54 (55.1)	43 (43.9)
Open-mindedness	2 (2.0)	91 (92.9)	5 (5.1)
Inquisitiveness	-	34 (34.7)	64 (65.3)

Contextual

High numbers of students (38) between ages 15-20 years are found in positive contextual CTD level. Majority of the students with matric from public sector school and FSc from private sector school are in positive level of contextual CTD.

Perseverance

Thirty students between ages 15-20 years are found in progressive perseverance CTD level. The female students are at progressive perseverance CTD score (46) as compared to male students (14), though male were less in number. Students who have completed their matric schooling from public and FSc from the private schools are progressive level. Furthermore, in term of mother and father occupation perseverance CTD scores are at progressive level.

Reflection

Forty-three students between ages 21-25 years are found in progressive reflection CTD level. The gender is strongly associated with reflection CTD levels. Female students are at progressive reflection CTD score (53) as compared to male students (27). Majority of students with

matric from public sector school and FSc from private sector school are in progressive level of reflection CTD. Furthermore, in term of mother and father occupation reflection CTD scores are at progressive level.

Intellectual-Integrity/Truth Seeking

The age was strongly associated with intellectual integrity CTD. Twenty-nine students between ages 21-25 years are found in progressive intellectual integrity CTD level. Female students showed positive intellectual integrity CTD score (37) as compared to male students (14). Majorly the students with matric from public sector school and FSc from private sector school are at progressive level of reflection CTD.

Creativity

The age was strongly associated with creativity CTD as well as its level. Thirty-three between ages 15-20 years are found in progressive creativity CTD level. Female students are more at the progressive creativity CTD scores (37) as compared to male students (17). The majority of the students with matric from public sector school and FSc from private sector school are at progressive level of creativity CTD. There is strong association between father occupation and creativity CTD score.

Inquisitiveness

Thirty-five students (35) age between 15-20 years are found in positive inquisitiveness CTD level. Female students have positive inquisitiveness CTD scores (40) as compared to male students (24). The majority of the students with matric from public sector school and FSc from private sector school are at positive level of inquisitiveness CTD.

Open – Mindedness

Majority of the students (47) age between 15-20 years are found at progressive open- mindedness CTD level. On the basis of gender, female students have positive open-mindedness CTD scores (62) as compared to male students (29). There is strong association between schooling backgrounds of matric with open-mindedness in Table 4.

The results indicated that the performance of students in FSc and BSN entry test was significantly associated with intellectual construct of CTD. While other CTD constructs including contextual perspective, perseverance, reflection, creativity, open-mindedness and inquisitiveness showed weaker association. The inter construct association of reflection was significantly associated with contextual and perseverance. The association of intellectual construct with contextual, perseverance and reflection constructs was significant. Students' score in open-mindedness was statistically significant associated with scores in contextual, intellectual and creativity constructs. The inquisitiveness was the only construct that has significant relationship with all the CTD constructs; contextual, perseverance, reflection, intellectual, creativity, open-mindedness, and inquisitiveness. The correlation scores indicated that overall CTD score was intermediately associated with the entire constructs of the CT in Table 5.

Table 4: Association of CTD constructs with demographic variables

Demographic Variables		Contextual		Perseverance		Reflection		Intellectual		Creativity		Inquisitiveness		Open mindedness	
		Mean ± SD	Sig.	Mean ± SD	Sig.	Mean ± SD	Sig.	Mean ± SD	Sig.	Mean ± SD	Sig.	Mean ± SD	Sig.	Mean ± SD	Sig.
Age	15–20 years	20.7 ±1.6	.050	26.1±3.2	.967	24.2±3.9	.079	35.9±3.8	.052	26.3±3.1	.056	37.3±3.3	.348	33.3±3.6	.771
	21–25 years	20.0 ±1.9		26.1±2.9		22.9±3.1		34.5±3.2		27.6±3.5		36.6±3.5		33.5±3.9	
Sex	Male	20.4 ±1.6	.940	26.4±2.9	.574	23.3±3.6	.599	35.4±4.0	.758	26.9±3.7	.862	37.0±3.0	.918	33.7±3.4	.588
	Female	20.4 ±1.9		26.0±3.1		23.7±3.6		35.2±3.4		27.0±3.2		36.9±3.6		33.3±3.9	
Matric	Public	20.4 ±1.7	.812	26.2±2.5	.804	23.2±3.7	.169	35.2±3.6	.775	27.2±3.4	.395	37.0±3.6	.959	34.1±3.1	.034
	Private	20.3 ±1.9		26.0±3.6		24.2±3.4		35.4±3.6		26.6±3.3		37.0±3.2		32.5±4.3	
FSc	Public	20.5 ±1.9	.596	26.2±2.8	.759	23.4±3.9	.702	35.2±3.8	.979	26.7±3.4	.979	36.8±3.6	.628	33.6±3.8	.732
	Private	20.3 ±1.8		26.1±3.2		23.7±3.3		35.3±3.4		27.2±3.4		37.1±3.3		33.3±3.7	
Mother occupation	House wife	20.6 ±1.7	.295	26.6±2.8	.077	24.0±3.5	.105	35.6±3.4	.199	27.2±3.4	.392	37.2±3.6	.789	33.8±3.6	.249
	Nurse	19.5 ±2.4		24.9±3.2		22.4±3.3		34.8±3.9		26.7±3.6		36.5±2.9		30.9±4.7	
	Teacher	19.9 ±2.0		25.0±3.5		23.3±4.1		33.0±3.6		25.5±3.3		36.6±3.1		32.7±2.8	
	Other	21.0 ±0.8		23.7±1.9		20.3±2.1		35.5±4.4		27.3±3.1		35.5±3.3		34.3±3.0	
Father occupation	Govt.	20.3 ±2.0	.925	26.3±2.3	.142	22.3±3.5	.182	36.4±3.3	.180	27.9±3.6	.045	37.4±3.4	.540	32.6±2.9	.112
	Private	20.5 ±1.8		26.9±3.1		24.0±3.9		35.1±3.6		25.4±3.4		36.8±2.8		32.6±4.1	
	Laborer	20.1 ±1.5		25.0±2.8		23.8±2.9		33.7±3.4		27.9±3.1		37.6±3.5		33.3±3.4	
	Business	20.5 ±1.5		25.8±3.0		23.2±3.6		36.1±3.5		27.5±2.9		36.9±4.1		34.3±3.7	
	Not working	20.5 ±2.0		26.4±4.0		24.5±4.1		35.9±4.0		27.5±3.5		35.5±4.0		36.0±2.9	

Table 5: Pearson's Correlation of FSc Marks and Entry Test with Constructs of CTD

		FSc Marks	Entry Test Marks	Contextual	Perseverance	Reflection	Intellectual Integrity	Creativity	Open mindedness	Inquisitiveness
Entry Test Marks	Pearson's R	0.530*								
	p value	0.001								
Contextual	Pearson's R	0.189	0.165							
	p value	0.063	0.105							
Perseverance	Pearson's R	0.089	0.091	0.140						
	p value	0.387	0.377	0.169						
Reflection	Pearson's R	0.109	0.092	0.341*	0.445*					
	p value	0.289	0.373	0.001	0.001					
Intellectual Integrity	Pearson's R	0.242*	0.223*	0.230*	0.316*	0.333*				
	p value	0.017	0.028	0.023	0.002	0.001				
Creativity	Pearson's R	-0.024	-0.064	0.035	0.125	0.017	0.080			
	p value	0.812	0.534	0.733	0.219	0.871	0.431			
Open mindedness	Pearson's R	0.090	0.062	0.331*	0.185	0.132	0.289*	0.273*		
	p value	0.382	0.544	0.001	0.069	0.197	0.004	0.007		
Inquisitiveness	Pearson's R	0.232*	0.171	0.282*	0.263*	0.250*	0.342*	0.361*	0.262*	
	p value	0.022	0.095	0.005	0.009	0.013	0.001	0.000	0.009	
Overall CTD Score	Pearson's R	0.218*	0.172	0.492*	0.598*	0.606*	0.646*	0.480*	0.613*	0.676*
	p value	0.032	0.092	0.001	0.001	0.001	0.001	0.001	0.001	0.001

Discussion

Critical thinking attitudes of nursing students were predominantly at the progressive level. These findings are consistent with international studies conducted in Korea at the being of educational programs.[13] Whereas another international study reported lower level of CTDs.[1] These findings have eminence that critical thinking disposition is at positive level in the start of their professional career, perhaps due to their curiousness and eagerness towards new knowledge, the other underpinning. Conversely, students who show low level of CTDs might have difficulty adjusting with the knowledge imparted to them or maybe they were less exposed to the problem solving and decision making.

The current study did not find the association of age with CTDs. Whereas a Korean study reported a positive relationship between age and the CTD.[13] The contextual differences in the educational system may have contributed to the CTD development among the Korean students. The previous studies have shown a variety of discrepancy regarding link of gender with CTDs which continue with the findings of current study reporting no association. This fact is further supported by no statistical significant difference of CTDs among male and female nursing students.[14] However, CTDs scores of female students were higher in current study aligning with a Brazil

study on undergraduate nursing students of year one, two and three has recognized that female exhibits positive in dispositions analyticity and maturity.[15] This fact may be a result of higher number of female samples in these studies.

The effect of students' previous education on CTDs is also debated in the literature. Aligning with an international study[16] no association was found in the current study. Critical thinking improves when students are engaged with active teaching and learning strategies.[17] However, despite of the research supporting that the benefits of utilizing different teaching learning strategies, nursing teachers are still utilizing traditional teaching learning strategies.[18]

Parenting role is considered important for the cognitive and behavioral development of the student. The present study found positive association between the mother's occupation and the CTDs. In Pakistani society, fathers predominantly play the role of bread winner whilst mothers assume a homemaker role. Therefore, mothers spend more time with the children which help them to develop critical thinking through motherly lens. Mothers rearing that is emotional warmth and understanding facilitate the development of CTDs.[19] Current study also found that students who have had high scores in their previous education performed better in the entrance test examination of nursing. Further there was moderate correlation between previous education and entrance test. Those who consistently scored higher also scored higher in the intellectual construct of CTDs. While high performance was associated with maturity and engagement in another study.[20] Perhaps internal consistencies of CTD construct affects each other. Therefore, high performing students could use different aspects of CTD to perform better.

The constructs of CTDs were evaluated to enlighten the depth of critical thinking among the nursing students. The systematicity construct was at progressive and positively associated with the FSc performance of the students. The contextual perspective was at the positive level and strongly associated with the age. As the age increase the exposure and experience also increase which leads to increase in contextual perspective of CTD. Among the seven subscales, intellectual integrity reported second highest score in this study and positively associated with gender, previous schooling type and age.

The intellectual integrity score was high of female and the students who studied previously from private schooling system. Further, the younger student intellectual integrity was high. Comparatively female comprises most of the study participants therefore results may have inclined toward them. The competition among the private schools to attract students stimulate them to use active teaching and learning strategies and providing them resources for the learning which help them to develop higher intellectual integrity. High score among younger age group in current study is contrary to other study.[1] The curiosity attribute to seek more information among younger may have contributed to the higher intellectual integrity. Regarding creativity construct of CTDs, the female students scored higher consistent with a Turkish study.[21] Same pattern was evident in reflection construct. Perhaps, female face more challenges during their upbringing. Majority of students in the current study scored higher in open-mindedness construct which consistent with study conducted in Istanbul.[1] These findings could be due to students being in their initial career, having a strong desire to learn, which propels them to accept others' views. In the current research an illuminated construct of CTD was inquisitiveness, and findings are consistent with international studies.[1,7,22] Female gender and those who studied FSc from private institution showed more inquisitiveness and the possible reason might be that they were exposed to innovative pedagogical strategies. The other reason could be their motivation towards learning increase inquisitiveness.

Strengths and limitations

The baseline data of critical thinking dispositions and its association with different demographic variables of neophyte was gathered in the Pakistani context. A follow-up longitudinal cohort and interventional studies could be conducted to develop CTDs among nursing and health profession disciplines. The tool used for data collection was developed in a Pakistani context and it was bilingual. The study was conducted on students from a private nursing institute, so the study findings are contextual, but could compare with private nursing colleges in Pakistan.

Recommendation

Institutions who envision their students a critical thinker should incorporate teaching, learning and assessment strategies potential to develop CTDs. Teachers are driving forces for this purpose. They should be prepared to impart and role-model CTDs. Longitudinal cohort and interventional studies may be conducted to evaluate the type of teaching, learning and assessment strategies would develop critical thinking dispositions. CT can be taught and developed in nursing students through various teaching, learning and assessment strategies.[23]

Conclusion

This study revealed the baseline data of nursing students' critical thinking dispositions which is at a progressive level. The CTD scores were higher for contextual perspective and inquisitiveness whereas lower in reflection and open-mindedness. Few students showed the negative critical thinking dispositions concerning reflection, intellectual integrity, creativity and open-mindedness therefore require educational strategies for improvement and possibility of interventional studies in the future. Of importance, the study highlighted significant association with previous education marks with CTD. Further, the intermediate correlation between the CTDs' constructs warrant, when one construct improves others would also improve producing a ripple effect. It is also believed that the findings can be used as guide to develop policy pertinent to CTD.

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ORIGINAL ARTICLE

Family caregivers' expectations and needs in Critical Care Units

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A B S T R A C T

Introduction: Patient admission into the critical care unit is usually an unpleasant and unexpected life experience for the family members. It is unusual for family members to cope with stress and anxiety during their hospital stay. Literature reveals that family members have distinct needs that must be recognized and met by the health care professionals to reduce their stress and increase their ability to support their patients.

Purpose: This study aimed to explore the expectations and needs of family members of the patients in critical care units at two tertiary care hospitals in Islamabad.

Methodology: An exploratory descriptive design was used to address the study questions. Using purposive sampling, 14 family members were individually interviewed through a semi- structured interview guide. A conventional content analysis method was used to analyze the data through which categories and sub-categories were identified.

Findings: The data analysis revealed three roles of the family members, which included assistance in physical care, facilitator in the provision of treatment and the decision maker. Among these roles, the former seems unique, but not surprising given the low nurse-patient ratio in the public sector of Pakistan. The participants expressed that their needs for information and assurance were being met to some extent; however, their need for support and comfort were not. Although the physical facilities for meeting the comfort were available in private hospital, it did not match the family members' expectations.

Conclusion: This study revealed that despite some similarities in the role and needs, the expectations and satisfaction of the family members is linked to their awareness of the healthcare system as well as the cost of the obtained services. The suggestions of the family members are implementable to improve their experiences and satisfaction in critical care units, which can enable them to perform their roles better.

Keywords: *Critically Care patients, expectations, experiences, family caregivers, needs.*

Introduction

Hospitalization in Critical Care Units (CCUs) has never been a pleasant experience, but always stressful and devastating. Admission in the critical unit is usually unplanned and occurs without warning to patients and their family members.[1] The CCUs deal with patients of high acuity, and uncertain outcomes that require complex care and are perceived as highly mortal places of the hospital. Due to this perception, admission of a beloved one in a critical care unit could be a highly threatening situation for the patients and their family members. [2]

Patients admitted to the CCUs may experience physiological stress due to their illness. Moreover, they may have psychological stress due to fear of unknown, loneliness and unfamiliarity with the environment of CCUs

and sometimes due to effects of medicines.[3,4] These 1 reasons make them incapable of making decisions. At this time, the family members are considered decision maker on the patient's behalf.[5]

Family members are the best source of providing support to the patients at the time of stress, but they generally experience psychological stress.[6-8] They are also frightened due to uncertain prognosis, fear of death or permanent disability of their patients.[9, 10] They may not be able to perform their role as supporter due to stress and anxiety related to their patient's prognosis and financial crisis during the stay at CCUs. If their concerns are not addressed, family members may face physical and psychological stress. They may experience feelings of helplessness and hopelessness.[11] Unaddressed stress of the family members leads to lack of trust towards the health care provider and this situation may result in noncompliance with the hospital rules, aggressiveness and lawsuits from family members.[12]

Literature reveals that during the time of serious illness, the family members of the critically ill patient have a unique set of needs.[13] These needs must be fulfilled to alleviate their anxiety and stress level; furthermore, fulfillment of such needs improve the satisfaction level of the family members with the care provision, promoting trust and assurance.[14] The emerging challenge for the critical care nurses is to take care of the patients along with meeting the needs of their family members. Assisting the family members to perform their role effectively in patient care the nurses must understand and address their needs.[15-17] However, as this research area has not received its due consideration in Pakistan so, there was a great need to explore this area.

Purpose of Study

The study was undertaken to answer the following questions:

1. What are the roles of family members of critically ill patients?
2. What are the needs of these family members?
3. What is their experience of meeting these needs?

Methodology

Study Setting and Sampling

This study was conducted from June to September 2018 in two tertiary care hospitals (one Public and one Private hospital) of Islamabad. Fourteen Family members were interviewed using purposive sampling.

Inclusion criteria

Family members of the patients who were admitted for more than 72 hours and were able to spend most of the time with their patients were considered eligible for interview.

Exclusion Criteria

The family members who were emotionally disturbed due to condition of their patients or unwilling to participate.

Ethical Consideration

The approval of Institutional Review Board of private hospital of the relevant University and permission for data collection were obtained from public hospital. The participants were assured that this participation is voluntary without any penalty or pressure. Furthermore, they were told that the dissemination of the findings will be done without revealing their identity.

Recruitment of participants

In both hospitals, the primary researcher obtained the list of admitted patient from the head nurse of the unit. The patients who were admitted since more than 72 hours were identified. Then the family members who were staying most of the time with the patients were recognized with the help of patients' bedside nurses. The family members were contacted with the help of head nurse either in the waiting areas or through a phone call. The head nurse informed the potential participants about the study and introduced the researcher. The participants were inquired individually about the extent of their interest and willingness to participate in the study.

Data Collection

Using an interview guide, face-to-face individual interviews were conducted to collect data. The demographic information of the family members including age, gender, and relationship with the patient, qualification, and occupation were obtained. The time spent with the patient was also noted. Each interview lasted for almost 30

minutes and was conducted in Urdu language except two or three participants who had used mixed language. During the interview, field notes were taken to note the gestures and expressions of the participants. Each interview was recorded and transcribed verbatim in Urdu and translated into English, and where appropriate the field notes were incorporated. Transcription of the interview was crosschecked with the recording for accuracy purpose.

Rigor of the study

The Rigor was ensured by following the criteria of trustworthiness given by Lincoln and Guba (1986) which include credibility, dependability, conformability and transferability. [18-20] The Table 1 below elaborates the features of the research that were considered while ensuring the criteria of trustworthiness.

Data Analysis

Data were analyzed manually by using the steps suggested by Mores and Richard.[21] Responses of all participants to each question were collected in one document. After this, the text was read several times before coding.[21] Relevant words and phrases from that document were then highlighted and coded for latent and manifest meaning such as; "The family members of patients suffer a lot" and "In fact this hospital is not providing any facility to the family members respectively. Following this, all similar codes were grouped together to generate categories and sub-categories through a cyclic reflective process.

Table 1: Rigors of the study

Criterion	Definition	Actions to ensure the criterion
Credibility	The credibility means the confidence in the truth of the data and their interpretation from sources Lincoln and Guba, (1986) [20]	• During the interview, the participants were encouraged to express their ideas openly. Clarification was sought in case of ambiguity. • Planned and unplanned probes were used for elaboration. • Reaffirming, repetition and expansion of question were done during the interview. • Field notes were taken in the form of non-verbal gestures.
Dependability	Dependability refers to the stability of the data over a period of time and in different settings and conditions Lincoln and Guba, (1986) [20]	• Transcripts were validated with the audiotaped interviews. • Data collection was stopped at or as? data saturation was achieved.
Conformability	Conformability refers to the objectivity, that is observed as an agreement between two or more people going through the findings to check for accuracy and meaning Lincoln and Guba, (1986) [20]	• Reflection on the information provided by the participants and confirming whether the information was the experiences or the ideas of the informant. • Employing latent and manifest content analysis. • Member check during and after the interview as and when required. • Excerpts from the participant's interview are used to support the analysis commentary.
Transferability	Transferability deals with the ability of the findings to be transferred to other settings or context Lincoln and Guba, (1986) [20]	• It is facilitated through a detailed description of the process. And, this would permit reader to decide the level to which the findings could be relevant to other settings. • A similar group of participants, in an identical context would yield comparable results if the process is repeated.

Findings

The analysis of participants' narratives was organized into two main categories which are; Roles of the family members and the needs and expectations of the family members. These categories are further divided 3 to 4 subcategories as depicted in the table below:

Table 2: Categories and sub-categories

Categories and Sub-categories

Categories	Sub-Categories	Examples
Roles of the family Members	Assistant in patient's *ADLs	Help the healthcare provider Provision of independent care
	Facilitator in patient's treatment	Run Errands Purchase Medicines / Supplies
	Decision maker for patient's treatment	
Needs and Expectations Along with Suggestions of the Family Members	Professional Behavior	Nurses/ doctors Allied staff
	Provision of information	
	Support & comfort	Physical Facilitation System Facilitation

*ADL- activities of daily living

The categories and subcategories are described in the proceeding sections and substantiated with excerpts from the participant's interviews. To improve their readability, the excerpts have been corrected to reduce grammatical errors, but without changing the intent of their responses.

1-Roles of the family members

Analysis of the participants' responses with regard to their roles revealed that they performed various roles; mainly as an assistant in patient's activities of daily livings (ADLs), facilitator in provision of treatment and being the decision maker for patient's treatment. Although the latter two roles were being performed by the family members in both hospitals, the role of assistant in (ADLs) was only expressed by the participants in the public hospital.

1.1 *Role of assistant in ADLs*

The participants explained that most of the times they assisted nurses in ADLs of their patients, but sometimes they were required to perform this role independently. As one of the participants expressed:

"I am helping him [patient] in moving, sitting and lying. I also move his bed accordingly [Just raise the head or making him comfortable]. I help the nursing staff to give the medications to my patient as they [nurses] guide. I am also helping him [my patient] to take his food" (AM- 02).

1.2 Facilitator in patient's treatment

Most of the participants shared that they facilitated their patient's treatment as per guidance of the healthcare providers (HCPs). They have to collaborate with the HCPs for the diagnostic tests of their patients not only inside the hospitals, but also outside the hospitals. A family member posited,

"Time to time we have to go for tests to different places such as, private labs for the tests which are not available in the hospital" (AM-01).

Some of the participants shared that they have to arrange blood and blood products for their patients. The family members revealed in their narrative that sometimes they have to purchase medicines for their patients. Although these responses were very few in number, but still it was considered bothersome for the family members. One of the study participants explained,

"They [doctors] have advised a medicine for my patient. This medicine is not available here in Pakistan. They [doctors] told me that drug is available in India, and I have to arrange it by my personal means" (BM-08).

1.3 Role of decision maker for patient's treatment

Participants' narratives revealed that most of the time doctors had informed them about the best solution to their patient's problem, but ultimate decision was left on the family members. One of the participants highlighted:

"The consultant of CCU called me in the unit and told me that my mother needs assistance in breathing, so he explained me all the possible outcomes and draw backs of the procedure [of artificial ventilator]. After explaining he asked me whether I will allow him [the doctor] to place my mother on ventilator or not" (BM-12).

2. Family member's needs and expectations along with their suggestions

While identifying their needs, the participants also articulated their expectations and to what extent these expectations were fulfilled. These expectations were varied from different health care providers; such as nurses, doctors and allied health staff.

The expressed expectations could be subcategorized into three areas; Professional Behavior; Provision of

information; Comfort and Support. Generally, the expectations were high in the private hospital and low in the public hospital.

2.1 Professional behavior of HCPs

Most of the family members reported that the professional behavior of nurses, doctors and other staff matters a lot. However, they have different expectations from the HCPs. Among all, most of their examples were related to nurses, and to some extent with the security guards. They also reflected on the responsibilities of nurses. They expect that the nurses must be competent, prompt, and cooperative. However, a few expressed that the behavior of nurses and doctors was not up to the mark. One of the participants shared,

"Nurses are responding to patient needs, but after 2-3 reminders" (AM-01).

The participants' expressed that sometime their expectations regarding the professional behavior of the HCPs were not being met. In contrast, some of the participants acknowledged the role and skills of the nurses.

As one participant eloquently summarized:

"The nurses are giving medicines, injections, and drips to the patients. They are performing cleaning of the respiratory tube [suction of the tracheotomy tube]. If they have time, they are helping us when we are involved in providing care to our patient" (AM-06).

While discussing the behavior of nurses, some participants also articulated the inappropriate behavior of doctors. As one of the participants expounded:

"One of my cousin sisters is doctor and she came to the CCU and asked about the results of laboratory tests from on duty doctor. He did not discuss anything with us and simply said that she [my cousin] can go to laboratory to receive those results. At least they can inform us that whether the results are normal or not" (BM-12).

Likewise, the participants' experience with doctors, nurses, and security guards was very similar at both hospitals. While sharing their experiences almost all of the participants complained against the unprofessional behavior of security guards.

"Security guard came and talked to me so rudely that even I could have slapped to him, but I controlled my anger. They even do not know how to talk to anyone. He did not allow me to sit on the sofa that was laying there in the lounge" (AM-01).

While discussing the behavior of security guards the participants proposed some suggestion to improve their professional behavior. As one of them proposed,

"The security guard should do his job according to his job description. The hospital must train these security guards for public dealing" (BM-09).

Except security guards their experience with other staff working at blood bank and laboratory was good. The participants of the study also highlighted some system errors which needs improvement. One of the participants expressed:

"The staff working in the blood bank is very nice, cooperative, and respectful especially Mr. ### [name] It was my first experience to donate blood for my patient, I never gave blood before this time, but he convinced me so nicely that I agreed to donate blood immediately" (AM-02).

2.2 Provision of information

Responses of the participant's revealed that although the information need was being met up to some extent, sometime the information was inadequate or was not being provided at all. Almost all the participants have expressed that most of the time the doctors are the ones who provide them information, but some of the participants also explained receiving information from nurses.

As one of the participants reflected:

"I know that my patient is not well enough. I know his progress and details of disease. The hospital staff-doctors and nurses told us all the details of my patient's disease from very first day and I know how much chances of recovery, my patient have?" (AM-01)

During the discussion, the participants of the study insisted on some points for the improvement of the information provision. A participant proposed,

"They must have an information policy. They can identify one or two persons from the family of patient and tell them about all situation in simple and easy to understandable terms" (BF-11).

2.3 Support and comfort

The participants of both hospitals revealed that their need for comfort and support was not being met. They shared several expectations indicating their requirement of

support and comfort. It was expected that waiting area must be cleaned, properly furnished with separate sitting arrangement for both males and females. The provision of toilets was considered most important as it is a basic human need. The participants of the study also expect that there must be an adequate place available for taking rest, especially at night. as one of the participants' reckoned,

"There is no place where patients' family members can sit. There is no proper space for them to take rest at night. We have to stay in the lawns of the hospital, which is challenging for us" (AM-01).

Another female participant articulated,

"The male and females have to stay together. There are too many males staying in this area. So, it is difficult for me and my relative [both females] here in between these male members" (AF-04).

The participants of the public hospital expressed that in fact they were not being facilitated at all. According to them the hospital was doing a lot for their patients, but they family members were suffering during their stay at hospital.

Although the family members of the private hospital acknowledged the facilitation of support and comfort; they wanted some improvement in those facilitation. The study participants in the private hospital shared that the facilities were available, but still some improvements were required to meet their needs. As one of them explained:

"There are some chairs in the waiting area. The sitting arrangement is good enough. The cooling system is fit. There is a canteen of tea and coffee. The waiting area is well furnished, but there is no place where someone can take rest especially in night" (BF-11).

Most of the participants were satisfied with their proximity level with their patients and they appreciated the hospital visiting policy.

Discussion

This study identified the needs and expectations of the family members of critically ill patients in tertiary care hospitals of Islamabad, Pakistan. The role of family members in decision making has been well reported in the international studies,[5,6] their contribution in the provision of care directly or indirectly was found unique to the current study. Moreover, the level of facilitation of the family members in the treatment of their patients was also more prominent in this study. The main factors that compel the family members assist patients' in ADLs in the public hospitals are lack of assistance in non-nursing tasks, and shortage of nurses. The shortage of nurses is well known in Pakistan; the nurse ratio patient is unfortunately very low.[16] The shortage of nurses was also acknowledged by the family members in this study.

It was gratifying that the family members were happy to be involved in the care. The findings of the current study can be utilized to enhance care provision in public sector. However, a systematic approach is required to organize the role of family care provider. In researchers' point of view, the capability of the family members for the identified tasks to be delegated must be assessed and ensured. Involving the family members in providing care could be beneficial, as they can help nurses by providing information regarding the wishes of their patients.[21]

Beside the shortage of nurses, in the public sector there is lack of assistance in non-nursing tasks. Unlike the private hospital, there is no concept of the respiratory therapists or technicians, unit receptionists, phlebotomists, nursing assistants and housekeeping staff in the public hospital. Therefore, in addition to the nurses' primary responsibility of patients care all the non-nursing tasks are being done by them. Thus, the nurses of the critical care units must perform the tasks that are not related to their cadre. Consequently, nurses are over worked in public sector due to shortage [22] and additional tasks. Employment of the nursing assistants and supporting staff may reduce nurses' workload and will be helpful to reduce the burden of the family members. [23-25]

Narratives of the participants have also indicated that sometimes due to lack of facilities or incase available facilities became out of order in the hospital, they were asked to seek services from outside the hospital. The family members not only found it difficult to coordinate with the outside facilities but perceived it as an extra financial burden on them. They expected that the hospital staff should perform these roles instead of the family members.

With regards to needs and expectations the finding of the study revealed that although most of the time the professional behavior of the nurses, doctors and allied health care staff was up to the mark, there were some instances of disappointment regarding non- professional

behavior of the nurses, doctors, and security guards. Most of the times the family members have trust in the care provided by the nurses as revealed in their narratives and they also acknowledged the contribution of nurses to their patients care. This finding was similar to the findings of a previous study in Pakistan which reported that nurses are considered hard working by the family members and that the hospital cannot work without them.[25]

Although the importance of nurses was well recognized by the family members, the need for improvement in the behavior was also expressed. In the current study the participants reported that sometime nurses were not able to respond to their patients' needs timely. In researchers' point of view this lack of promptness can be explained to some extent by the workload and associated stress[16] in the nurses. While nurses working in public hospitals in Pakistan are stressed due to being overworked and nurses working in the private sector are under stress due to excessive accountability,[16] so these reasons may affect their behavior.

The study participants highlighted the inappropriate behavior of the security guards explicitly. Security guards of the hospital are responsible to control the crowd in the hospital. Family members and friends come to visit their patients according to their ease. In addition, the number of the visitors is high which is aligned with the cultural and religious norms in Muslim society.[2] Given the low literacy rate in Pakistan, family members may not respond well when they are controlled because they do not want to follow the rules and keep insisting to visit their patients. These reasons make it difficult for security guard to control them. Moreover, the security guards may not be professionally trained for public dealing.

With regards to the needs and expectations this study identified that family members' need of information was being met up to some extent. International studies indicate that family members always appreciated when the need for information was being met.[3,19] A study in Pakistan also indicated that 85.0% of the participants rated provision of information as their most important need.[22] The information provision or communication with the family members of critically ill patients in Pakistan remains a grey area,[26] the participants in the current study also shared that they wanted improvement in information provision. The family members expected and required information related to treatment, prognosis, and important decisions. Similar to a study in Hong Kong,[27] in the current study, the need for provision of information was mostly addressed by the physician, but to a limited extent by nurses, which is contrary to the role of nurses, because their availability is more extensive at bedside.

Physical facility and comfort is also a significant need of family member, whether in Pakistan or elsewhere, contrary to the international literature,[26, 27] in the current study the family members mentioned several issues particularly related to the facilities available to them, these issues were more prevalent in the public hospital; as facilities like comfortable chairs, adequate but separate place for males and females, fans, toilets and space for taking rest at night were non existing there. It was reported that most of the times the males and females had to stay together. Considering the cultural aspects of Pakistan, it was evident that participants were highly uncomfortable in staying together in common waiting room. Although these facilities in the private hospital were good, but the expectations of the family members were high because they were paying for that. The findings of the current study warrant the need to develop strategies that may enhance the comfort of the family members, particularly in the public hospitals.

Although this study provided an in-depth understanding of patients' family members' needs in two tertiary care hospitals, the researchers believes that the knowledge gained from this study may be of some benefit to nursing practice, education, and future research. Meeting the needs of the family members will not only reduce their anxiety level, but also build confidence of family members in the healthcare system and ultimately improve health outcomes.[28, 29] Implementation of the current study findings on institutional level will enhance the understanding of the needs of family members that can provide a foundation for improving their services. Several suggestions given by family members can be easily incorporated in the hospitals to enhance their comfort and consequently their contribution in the care of their patients' recovery.

Conclusion

This study focused on the identification of the needs of family members. Although the needs related to information, support and proximity were being met up to some extent; the need for comfort was not being met especially at the

public hospitals which calls for attention by the leaders and administrators in the healthcare sectors.

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ORIGINAL ARTICLE

Effect of sleep quality on academic performance of undergraduate University level students

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[1] Conceptualization analysis and interpretation of study,
[2] Investigation, data analysis, drafting
[3] Conceptualization analysis, Drafting, Interpretation of study
[4] Conceptualization analysis, critically revising the study
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A B S T R A C T

Introduction: Memory processing and learning are enhanced by adequate, high-quality sleep of the appropriate duration. It aids memory processing, executive cognitive functioning and concentration. Academic performance of university students suffers as a result of poorer sleep quality.

Objectives: To determine the effect of sleep quality on academic performance of undergraduate university level students.

Methodology: This is analytical cross-sectional study and non-probability purposive sampling technique was used. The study population comprised a total 300 students, out of which 50 students were not completed the questionnaire. A total of 250 students, 113 male and 137 female students were participated in this study. A structured questionnaire was circulated among bachelor-level students of different universities in blinded from August 2018 to December 2018. The questionnaire was based on Pittsburgh Sleep Quality Index along with other relevant data about the students' age, gender, and discipline of study, respective semester and grades (CGPA or percentage total). The data obtained was analyzed using SPSS 21.

Results: Majority of the students had moderately poor sleep quality (Global PSQI score=5). The 17.6% of subjects scored 5 in PSQI and 14.8% of subjects scored 6 in PSQI. However, the students who scored high CGPA (>3.5) had better sleep quality as compared to those who got CGPA <3.5.

Conclusion: Majority of the students having poor sleep quality and their grades might be affected. Furthermore, the students who attaining good CGPA (>3.5) had on an average good sleep quality.

Keywords: *Academic performance, NREM, PSQI, REM, sleep quality, University students*

Introduction

Sleep and wakefulness, the two basic processes of life, are like two different worlds with independent controls and functions. As we age, humans keep on transforming and adapting different phases of sleep.[1] During different times of the day from dawn to dusk, human body switches on between wakefulness and sleep. Deviations from this circadian rhythm come with functional consequences. According to a study about 17 hours of constant wakefulness leads to decrease in average performance of student.[2] Around 50–70 million US adults suffer from sleep disorders worldwide.[3]

Sleep deprivation is generally classified into three categories; total sleep deprivation; the complete lack of sleep for at least one night and often longer, partial sleep

deprivation; restricted sleep for multiple nights and the third category is sleep fragmentation; repeated awakenings from sleep throughout the night.[4] There are certain effects of sleep deprivation on academic performance of university going students in which brain responses decrease in persistent attention demands, reduced performances on constant attention activities and also decreased activation of specific brain areas as compared to well rested state.[5]

Evidence suggest that female students are at high risk of developing sleep disorders besides men.[6] Many college students are at risk for sleep disorders, and those at risk may also be at risk for academic failure.[7] Undergraduate university level students suffer from sleep deprivation due to a lot of factors that result in sleepiness during working hours.[8] It is also understood that many students are themselves unaware of their sleep deprivation or poor sleep quality. They may not seek counseling or advice regarding this important problem.[9]

Multiple studies have been conducted in order to find out the relationship between academic performances of student's and the results suggest that Sleep deprivation and poor sleep quality are common among undergraduate university level students. High levels of stress and the pressure of maintaining grade point averages may be influencing their quality of sleep.[10]The academic performances of different years of students vary as their ability to adapt to their study hours and accurate management of stress establishes.[11]

Excessive daytime sleepiness (EDS) is common among university students and has many adverse consequences, out of which academic performance is the one that is affected the most.[12] There are certain factors important to score high grades in exams i.e., declarative knowledge, procedural knowledge, cognitive processing and memory. Some other factors are vigilance, attention span, ability to concentrate over long periods of time, ability to retain information and memory consolidation.[13] Sleep quality effects all these parameters in some way and hence it remains an important factor affecting academic performance and grades of students. Sleep quality is a potent factor of sleep wake patterns and daytime functioning, performance on university tests and exams is one of these days' time functions. Poor sleep quality has been found to be associated with poor academic achievement and health, as well as increased health care costs and absenteeism from work.[14]

This study was initiated to describe the effects of sleep quality on academic performance of undergraduate university level students. With this study, awareness can be raised about effect of sleep quality on academic performance.

Methodology

This analytical cross-sectional study was conducted from different universities across Rawalpindi and Islamabad, Pakistan. The universities from which data was collected include National University of Science & Technology (NUST), Foundation for Advancement of Science and Technology (FAST), Riphah College of Rehabilitation Sciences (RCRS) Riphah International University, Foundation University Medical College (FUMC), Shaheed Zulfiqar Ali Bhutto Institute of Science & Technology (SZABIST) and SKANS School of Accountancy. Sample size was calculated as 300 by using Rao soft keeping the margin of error 5% and 95% confidence interval and response distribution rate was 50% through Purposive non probability sampling technique out of which 50 students were not completed questionnaire. The total of 250 students 113 male and 137 female students were participated.

The details were recorded through a structured Questionnaire "Pittsburg Sleep Quality Index" The Pittsburgh Sleep Quality Index (PSQI) is an effective instrument used to measure the quality and patterns of sleep in adults. It differentiates "poor" from "good" sleep quality by measuring seven areas (components): subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medications and daytime dysfunction over the last month.[15] The PSQI global score has a possible range of 0-21 points, 0 indicating no difficulty and 21 indicating severe difficulties in all areas. This self-reported questionnaire was given to selected students. Consent was taken from all the participants and confidentiality was ensured. Participants with history of any chronic illness and drug abuse were excluded from the study. The survey was conducted from August, 2018 to December, 2018. The descriptive analysis of data was done through SPSS 21.

Results

A total of 250 students from various universities filled out the questionnaire, out of which 106 students belonged to medical & health sciences, 109 students to engineering and 35 students to management sciences. Out of total 250 students who completed the questionnaires, 113(45.2%) were males and 137(54.8%) were females. Effect of sleep quality on scores of students has been shown in graph 1. The graph shows that greater number of females scored higher on PSQI as compared to males. Hence it can be inferred that females have slightly poorer sleep quality as compared to males.

All the respective institutions taken have same CGPA min/max criteria. Academic performance was assessed by asking participants about their cumulative grade point average (CGPA). Participants provided their CGPA for the last semester prior to the study period; the CGPA ranged from 1 to 4 points. Subjective sleep quality was based on the self-rating of students of their sleep quality. Students rated their sleep quality from very good to very bad. Majority of the students (n=126) with 50% had a 'fairly good' subjective sleep quality and 76(30.4%) had 'very good' subjective sleep quality. Only 14 (5.6%) students had 'very bad' subjective sleep quality as shown in Table 1.

According to the results, maximum number of students (95) lied in the CGPA group 3.0-3.4. The subjective sleep quality of this group of students was such that, 25 students had 'very good', 47 had 'fairly good', 17 had 'fairly bad' and only 6 students had 'very bad' subjective sleep quality. Secondly, a total of 60 students had CGPA ranging from 2.5 to 2.9 and their results showed 15 students had 'very good', 32 had 'fairly good', 7 had 'fairly bad' while only 6 had 'very bad' subjective sleep quality. The third largest group according to CGPA was of the 47 students who got CGPA from 3.5 to 3.9, of which, 18 students had 'very good', 24 had 'fairly good', 4 students had 'fairly bad' while only 1 had 'very bad' subjective sleep quality. From these results we can infer that, maximum number of students got CGPA from 2.5 to 3.9 and according to subjective sleep quality, maximum 126 students claimed to have 'fairly good', 76 said to have 'very good' 34 said to have a 'fairly bad' and only 14 claimed to have 'very bad' subjective sleep quality as shown in Figure 2. Pearson correlation was used to determine the effect sleep quality on academic performances. There was a positive correlation between the two variables, between sleep quality and academic performance r = 0.35, P = 0.04. Students who have very good sleep quality were more likely to have higher mean CGPA as compared to those who have fairly bad or very bad sleep quality.

Table 1: Frequency and percentages of Student's grades and sleep quality (n=250)

Student's (CGPA)	Frequency (n)	Percentage (%)
0.1 – 1.4	2	0.8
1.5 –1.9	3	1.2
0.2 – 2.4	21	8.4
2.5 – 2.9	60	24.0
3.0 – 3.4	95	38.0
3.5 – 3.9	47	18.8
4.00	22	8.8
Total	250	100.0
Sleep quality		
Very Good	76	30.4
Fairly Good	126	50.4
Fairly Bad	34	13.6
Very Bad	14	5.6
Total	250	100.0

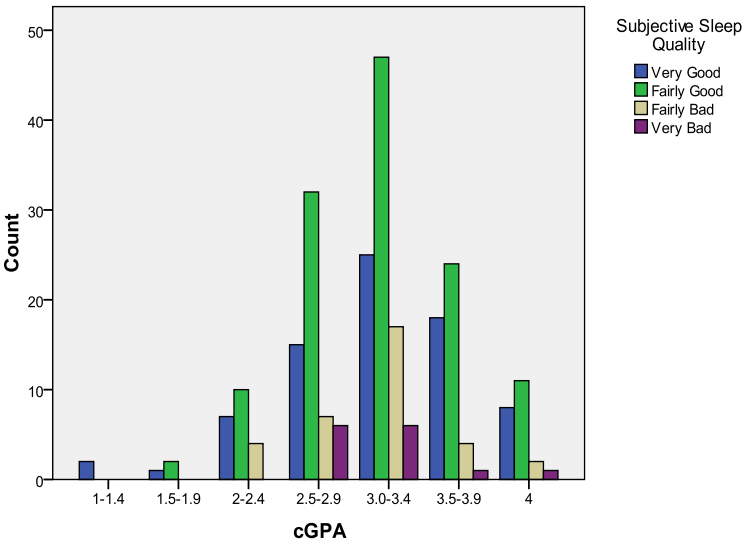

Figure 1: Effect of sleep quality on the grades CGPA of students

Discussion

According to the results of our study, females scored higher on the PSQI hence it can be said that females have a poorer sleep quality as compared to males. Although the difference is not very notable, females have a sleep quality slightly inferior to males. Some studies support this result while some show gender does not play a role in determining sleep quality. A study by Lindberg et al supports the fact that females have poorer sleep quality as females experienced difficulties in maintaining sleep, had episodes of morning tiredness and frequent daytime napping. Cheng et al, also supported the fact that females have a poorer sleep quality.[16] On the other hand, studies by Wolfson and Carskadon, 1998; Tsai and Li, 2004; Kadison, 2005 showed that there was no difference in sleep quality in women and men. However small sample size and methodological differences may be the reason of varied results. Hence the role of gender in this regard remains unclear.[17]

The result of our study showed that the majority of students got CGPA above 3.0 and the PSQI score was ranging from 3 to 10. However, one notable finding was the students who got exceptionally high CGPA (3.5-3.9) had a better sleep quality as compared to those with CGPA less than 3.5. Moreover, the comparison of CGPA with all the components of PSQI showed that students with higher CGPA had fewer difficulties in components of sleep quality as compared to those with lower CGPA. Many studies suggest that sleep has a definite effect on school performance and grades of students. Meijer AM et al in their study concluded that chronic sleep deprivation has a definite effect on cognition that in turn affects the school performance of students. The study suggested that sleep duration and sleep quality had different effects on cognition and academic performance.[18]

A study on the performance of medical students by Ahrberg K et al., suggested that low sleep quality did not necessarily contribute to academic performance. He showed in his results that students who received poor grades did not have a poor sleep quality or a high stress level. He suggested that most medical students preparing for exams suffer high stress levels and poorer sleep quality but their grades do not correlate with the stress level or sleep quality.[19] A study suggests that the insufficient or disturbed sleep manifests itself in the form of daytime sleepiness.[18]

The comparison of CGPA with all the components of PSQI showed that students with higher CGPA had less difficulty in components of sleep quality as compared to those with lower CGPA.[20] In another study the prevalence of poor sleep quality among the population has been reported to be 26–35% using the Pittsburgh Sleep Quality Index (PSQI).[21]

Conclusion

Based on the findings of current study, it is concluded that the CGPA (Cumulative Grade Points Average) falls as the sleep quality deteriorates. Furthermore, the students attaining good CGPA (>3.5) had an average good sleep quality.

Limitations

As academic performance and PSQI questionnaire was filled by students themselves, it is not clear whether the errors from self-reporting were random or systematic.

Recommendations

It is hence recommended that university level students should pay special attention toward their sleep hygiene. Proper hours of sleep along with other components of sleep quality should be taken care of. Sleep quality related to depressive symptoms affecting the grades of students can also be studied. Study can also be done within students of same discipline. Further study can be done on this subject with a larger sample size and using multiple tools for assessing sleep quality.

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ORIGINAL ARTICLE

Knowledge, attitude and practices study regarding current COVID-19 pandemic in patients presenting to rheumatology clinic of a Tertiary Care Hospital

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A B S T R A C T

Introduction: The most important step in controlling the spread of any communicable disease is to stick to preventive measures and COVID-19 pandemic is no exception. Simple measures like wearing a mask, regular hand hygiene, disinfecting the surfaces can significantly reduce the spread of the disease. Keeping this in mind, a KAP study was performed in the rheumatology unit of a tertiary care hospital of Islamabad. The main idea was to know the level of understanding of rheumatologic patients with respect to COVID-19 pandemic and its preventive measures.

Objective: The objective of the study was to understand the knowledge, attitude and practices of rheumatologic patients towards COVID-19 pandemic.

Methodology: A descriptive cross-sectional study in which consecutive, non-probability sampling technique was used.

Results: There were 37 males and 73 females in the study group, with mean age of 38.75±13.9 years.

The total knowledge score was 17 points. It was found that 12 (10.9%) participants had poor knowledge regarding COVID-19, whereas 27 (24.5%) and 71 (64.5%) had good and excellent knowledge respectively. The total attitude score of study participants 7 points. It was found that 11 (10.0%) participants had poor attitude, whereas 72 (65.5%) and 27 (24.5%) had good and excellent attitude. The total practice score was 11 points. It was calculated that 30 (27.3%) study participants had poor practices regarding COVID-19 prevention, whereas 78 (70.9%) had good practices and only 2 (1.8%) had excellent practices.

Conclusion: Overall, it was noted that KAP of our rheumatologic patients towards COVID-19 infection was reasonable, however, there is always room for improvement.

Keywords: *Attitude, COVID-19, knowledge, pandemic, rheumatology*

Introduction

One of the greatest tragedies the world has faced in recent times is the COVID-19 pandemic. The virus was first detected in the fourth quarter of 2019 in Wuhan, China. It was initially known as "Wuhan Coronavirus".[1] In February 2020, the virus was named COVID-19 virus by the WHO.[2] Information flowing out of China was initially slow and by the time Wuhan went into a lockdown and other countries reacted by banning travel to and from the China, it was already too late.[3] Within weeks, the virus had spread to multiple countries across the globe, making it a pandemic that could rival the scale and impact of the Spanish flu of 1919.[4] The first wave spread quickly to Europe and North

America, and from there, to the rest of the world.[5] The disease exhibits variable symptoms, ranging from mild to severe. Common symptoms are headache, sore throat, nasal congestion, cough, loss of smell and taste, shortness of breath, diarrhea and body aches etc. Around 81% of the patients develop mild while 14% develop severe symptoms.[6] It is not well established how many people are infected by one person but is estimated that about 10-20% of infected people are responsible for the disease spread.[7] The mode of spread is through droplets that pass from one person to another via respiratory route.[8]

Due to its rapid spread, the disease (word omitted) tested the capacity of healthcare systems around the world. Even in developed countries like Italy, Spain, UK and the U.S, hospitals were overwhelmed during the first and second waves of the pandemic, resulting in deficiencies in critical care and many casualties that could have otherwise been prevented.[9] In developing countries like India and Brazil, the impact was tragic. Provision of basic services like oxygen cylinders came under severe stress and critical care was denied even in major cities like New Delhi. India alone witnessed more than 29 million confirmed cases and 367,097 deaths.[10]

The unvaccinated people can protect themselves by wearing a mask, maintaining a distance of 6 feet in public places, avoiding crowded place and washing hands periodically.[11] In countries where the population generally adhered to preventive measures, incidence of infection and deaths was notably low. For example, China and New Zealand, where Governments imposed strict social restrictions and implemented lockdowns where necessary, less than 600 confirmed cases per-one million of population were observed.[12]

With the discovery of the vaccine against the virus and mass vaccination, there is a hope that the burden of the disease will significantly reduce in the months to come.[13] It has been noted that certain co-morbidities make the patients more susceptible to poorer outcomes of COVID-19 infection[14] as does the weak immune system like we see in cases of patients suffering from different rheumatologic diseases. The presumed risk of corona virus related complications in this population is so high that different national and international societies for rheumatology have issued guidance for doctors on how to stratify patients suffering from different rheumatologic diseases into low, moderate and high risk groups and what guidance to give to these patients as regards self-isolation and maintaining social distance.[15] Doctors all over the world are highly cognizant of the need for proper counselling of patients in this regard and Pakistani doctors are no exception. Keeping in mind this whole scenario, this KAP study was conducted in the rheumatology unit of a tertiary care hospital of capital city Islamabad. The main idea was to know the level of understanding of our patients with regards to the current COVID-19 pandemic and their adherence to the SOPs laid for the prevention of the spread of the disease.

Methodology

This descriptive cross sectional observational study was conducted in a Rheumatology unit of Federal Government Polyclinic Hospital Islamabad from 15th February 2021 till 15th April 2021.The sample size was 110 which was calculated using WHO calculator taking the prevalence of rheumatic disorders as 5-8% of the whole population with a confidence interval of 95% and standard error of 5%. All patients suffering from different autoimmune rheumatologic diseases presenting to rheumatology OPD or admitted in Rheumatology ward were included in the study. The data was collected after taking an informed consent from the patients.

The questionnaire had three components containing questions related to Knowledge, Attitude and Practices about COVID-19 pandemic. IBM SPSS (version 23.0) software was used for data entry and analysis. Descriptive statistics were presented as frequency and percentage for qualitative variables, while mean and standard deviation was used for quantitative variables. The knowledge, attitude and practice mean scores were compared between different groups using independent samples T-test. Multivariate analysis was done for significant predictors to draw association with knowledge, attitude and practices in terms of odds ratio, 95% confidence interval and p-value. A p-value of ≤0.05 was considered statistically significant.

Results

There were 37 (33.6%) males and 73 (66.4%) females in the study group, with mean age of 38.75±13.9 years and an age range of 13-70 years. There were 20 (18.2%) participants with no education, 71 (64.5%) were

undergraduates while 19 (17.3%) were graduates. Out of one hundred and ten participants, 44 (40.0%) belonged to low socioeconomic group whereas 66 (60.0%) had middle socioeconomic status. In terms of employment, about 39 (35.5%) participants were working, 55 (50.0%) were non-working and there were 16 (14.5%) students. Rheumatoid arthritis was the most common disease condition affecting around 77 (70.0%) of the participants, followed by systemic lupus erythematosus 8 (7.3%). Regarding drug treatment, methotrexate was the most commonly used drug in 63 (57.3%) patients, followed by leflunomide 13 (11.8%) and sulfasalazine 12 (10.9%). There were 10 (9.1%) patients on biological Disease Modifying Anti-Rheumatic Drugs, and 51 (46.4%) were on steroids. In terms of COVID-19 infection, only 2 (1.8%) patients had a history of COVID-19 infection. The sociodemographic characteristics of study population are summarized in Table 1.

The mean knowledge score of study participants was 12.2±1.8, from a maximum of 17 points. It was found that 12 (10.9%) participants had poor knowledge regarding COVID-19, whereas 27 (24.5%) and 71 (64.5%) had good and excellent knowledge respectively as shown in Figure 1. There were 88 (80.0%) participants who agreed that COVID-19 exists, while remaining 22 (20.0%) were in denial. Fever was the most common symptom of COVID-19 as reported by 42 (38.2%) participants followed by fatigue/malaise 21 (19.1%) as shown in Figure 2. Around 48 (43.6%) agreed that there is no pertinent treatment for COVID-19, while 34 (30.9%) disagreed and 28 (25.5%) were not sure. Majority of the participants, 110 (90.1%), were aware of correct route of infection transmission. Almost all of the participants (99.0%) reported that wearing mask when leaving home can prevent spread of infection in general population, similarly 97.3% were aware that by avoiding going to crowded places the infection transmission can be stopped. Detailed responses of COVID-19 knowledge are given in Table 2.

The mean attitude score of study participants was calculated to be 4.8±1.0, from a maximum of 7 points. It was found that 11 (10.0%) participants had poor attitude, whereas 72 (65.5%) and 27 (24.5%) had good and excellent attitude regarding COVID-19 pandemic. Majority of the participants, 100 (90.9%), were aware of the fact that unnecessary visits to the hospital should be avoided during COVID-19 pandemic. The monthly income of 67 (60.9%) got affected due to lockdown. Half of the participants, 58 (52.7%), reported that stress due to COVID-19 situation has mostly affected their lives, followed by financial issues 23 (20.9%) and lack of social life 19 (17.3%). It was reported by 50 (45.5%) participants that they will get vaccinated for COVID-19- if government would offer it as shown in Table 3.

The mean practice score of study participants was found to be 6.7±1.5, from a maximum of 11 points. It was calculated that 30 (27.3%) study participants had poor practices regarding COVID-19 prevention, whereas 78 (70.9%) had good practices and only 2 (1.8%) had excellent practices. Majority of the participants, 104 (94.5%) reported that they wear masks whenever they go outside and 85 (77.3%) maintains social distance of six feet. Around 38 (34.5%) participants were still going to crowded places like mosques, markets, weddings etc. during lockdown. Half of the participants, 48 (43.6%) thought that those with symptoms of COVID-19 should immediately report to the hospital while other half 53 (48.2%) said that they should isolate themselves at home. Majority of the participants, 94 (85.5%), were avoiding shaking hands with people during COVID-19 pandemic as shown in Table 4.

Univariate analysis of knowledge and practices score revealed no significant association with sociodemographic characteristics including age, gender, education, employment and socioeconomic status. In context of attitude score, significant relationship was found with education level and socioeconomic status as shown in Table 4. Participants with higher level of education had a better attitude score (p=0.036), similarly those with better socioeconomic status had a better attitude as compared to those with low socioeconomic status (p=0.018). A significant correlation was found between knowledge and practice score, which means that those with good knowledge of COVID-19 were more likely to follow good practices for preventing spread of COVID-19 where the coefficient of correlation was calculated to be 0.3 (r=0.3, p=0.002) as shown in Figure 3.

Score revealed no significant association with sociodemographic characteristics including age, gender, education, employment and socioeconomic status. But a significant correlation was found between knowledge and practice score, which means that those with good

knowledge of COVID-19 were more likely to follow good practices for preventing spread of COVID-19 (r=0.3, p=0.002) as shown in Figure 3.

Table 1: Sociodemographic and clinical characteristics of study population (n=110)

Sociodemographic & clinical characteristics	Frequency/Percentage N (%)	
Age in years (mean±SD)	38.75±13.9	
Age range	13 – 70	
Gender	Male	37 (33.6%)
	Female	73 (66.4%)
Education level	Illiterate	20 (18.2%)
	Undergraduate	71 (64.5%)
	Graduate	19 (17.3%)
Socioeconomic status	Low	44 (40.0%)
	Middle	66 (60.0%)
Working status	Students	16 (14.5%)
	Employed	39 (35.5%)
	Unemployed	55 (50.0%)
Diagnosis	Rheumatoid Arthritis	77 (70.0%)
	Systemic Lupus Erythematosus	8 (7.3%)
	Gout	3 (2.7%)
	Ankylosing Spondylitis	5 (4.5%)
	Enthesitis related JIA	8 (7.3%)
	APLS	6 (5.5%)
	Dermatomyositis	3 (2.7%)
Treatment	Methotrexate	63 (57.3%)
	Sulfasalazine	12 (10.9%)
	Leflunomide	13 (11.8%)
	Hydroxychloroquin	7 (6.4%)
	Secukinumab	3 (2.7%)
	Mycophenolate mofetil	6 (5.5%)
	Eternacept	6 (5.5%)
Biological DMARDs	Yes	10 (9.1%)
	No	100 (90.9%)
Steroids	Yes	51 (46.4%)
	No	59(53.6%)
History of COVID-19 infection	Yes	2 (1.8%)
	No	108 (98.2%)

Table 2: Frequency/percentage of responses by the study participants for knowledge questions (n=110)

Sr.	Knowledge Questions	Frequency	Percentage
1.	Does COVID-19 pandemic exist?		
	• Yes	88	80.0%
	• No	22	20.0%
2.	There is no treatment for COVID-19?		
	• Yes	48	43.6%
	• No	34	30.9%
	• Not sure	28	25.5%
3.	ALL the patients have serious disease?		
	• Yes	30	27.3%
	• No	58	52.7%
	• Not sure	22	20.0%
4.	Who are prone to COVID-19 infection?		
	• People of all age groups	63	57.3%
	• Children and old people	35	31.8%
	• People with pre-existing illnesses	12	10.9%
5.	What is the main transmission route of COVID-19?		
	• Water	5	4.5%
	• Respiratory droplets	56	50.9%
	• Infected fomites	27	24.5%
	• Close contact	17	15.5%
	• Not sure	5	4.5%
6.	Does it spread by touching the clothes or fomites of infected person?		
	• Yes	89	80.9%
	• No	16	14.5%
	• Not sure	5	4.5%
7.	Does every infected person need hospitalization and oxygen?		
	• Yes	36	32.7%
	• No	68	61.8%
	• Not sure	6	5.5%
8.	Can a person stay asymptomatic after catching COVID-19 infection?		
	• Yes	41	37.3%
	• No	51	46.4%
	• Not sure	18	16.4%
9.	Does wearing a mask prevent the general population from its spread?		
	• Yes	109	99.1%
	• No	0	0%
	• Not sure	1	0.9%
10.	To prevent the spread of infection avoiding crowded places is necessary?		
	• Yes	107	97.3%
	• No	3	2.7%
11.	Isolating the infected person and treating them helps prevent further people getting the infection?		
	• Yes	97	88.2%
	• No	9	8.2%
	• Not sure	4	3.6%

12.	Contacts of infected persons should be isolated for how many days?		
	• 10 days	6	5.5%
	• 14 days	87	79.1%
	• Not sure	17	15.5%
13.	Does washing hands, using mask and observing social distancing decrease the spread?		
	• Yes	108	98.2%
	• No	2	1.8%
14.	Are you at a greater risk of having COVID-19 infection because of your disease?		
	• Yes	53	48.2%
	• No	39	35.5%
	• Not sure	18	16.4%
15.	Was there any difficulty in getting the medication you are on because of COVID-19?		
	• Yes	25	22.7%
	• No	85	77.3%
16.	Do you think your medications make you more prone to have the disease?		
	• Yes	2	1.8%
	• No	1	0.9%
	• Not sure	107	97.3%

Table 3: Frequency/percentage of responses by the study participants for attitude questions (n=110)

Sr.	Attitude Questions	Frequency	Percentage
1.	Should people avoid unnecessary visits to the hospitals?		
	• Yes	100	90.9%
	• No	10	9.1%
2.	How has it impacted your life?		
	• Financially	23	20.9%
	• Lack of social life	19	17.3%
	• Compromised studies	10	9.1%
	• Stress	58	52.7%
3.	Has your monthly income been affected by the COVID-19 pandemic?		
	• Yes	67	60.9%
	• No	39	35.5%
	• Not sure	4	3.6%
4.	Do you think lockdown is good to prevent spread of COVID-19 infection?		
	• Yes	85	77.3%
	• No	21	19.1%
	• Not sure	4	3.6%
5.	Are Pakistanis more immune to COVID-19 infection?		
	• Yes	82	74.5%
	• No	14	12.7%
	• Not sure	14	12.7%
6.	Pakistan is in a good position to contain COVID-19 pandemic?		
	• Yes	89	80.9%
	• No	12	10.9%
	• Not sure	9	8.2%
7.	If offered, will you get yourself vaccinated against COVID-19?		
	• Yes	50	45.5%
	• No	47	42.7%
	• Not sure	13	11.8%

Table 4: Frequency/percentage of responses by the study participants for practices questions (n=110)

Sr.	Practices Questions	Frequency	Percentage
1.	Do you use mask when you go out?		
	• Yes	104	94.5%
	• No	5	4.5%
	• Sometimes	1	0.9%
2.	Do you maintain social distance of six feet?		
	• Yes	85	77.3%
	• No	24	21.8%
	• Sometimes	1	0.9%
3.	Have you stopped taking your medicines because of fear of the COVID-19?		
	• Yes	5	4.5%
	• No	105	95.5%
4.	Do you still go to crowded places?		
	• Yes	38	34.5%
	• No	72	65.5%
	If yes, then where? (n=38)		
	• Mosque	16	42.1%
	• Wedding	6	15.7%
	• Market	11	28.9%
	• Visiting relative	5	13.1%
5.	Do you wash your hands frequently now?		
	• Yes	102	92.7%
	• No	5	31.8%
	• Not sure	3	22.7%
6.	How frequently do you wash your hands?		
	• Every 2 hours	50	45.5%
	• Every 4 hours	35	31.8%
	• Only after using the toilet	25	22.7%

7.	If someone has symptoms, what should they do? • Isolate themselves at home • Wear mask and do normal activities • They should go to hospital	 53 9 48	 48.2% 8.2% 43.6%
8.	Do you touch your face and eyes with unwashed hands after touching any surface outside home? • Yes • No • Not sure	 17 86 7	 15.5% 78.2% 6.4%
9.	For you the most common barrier for using protective measures is? • Social stigma • Lack of resources • Inaccessibility of protective measures • There is no protective role of these measures in spread of disease	 36 49 16 9	 32.7% 44.5% 14.5% 8.2%
10.	Are you keeping food reserves at home? • Yes • No	 40 70	 36.4% 63.6%
11.	In recent days have you avoided shaking hands with people? • Yes • No	 94 16	 85.5% 14.5%

Univariate analysis of knowledge and practices score revealed no significant association with sociodemographic characteristics including age, gender, education, employment and socioeconomic status. In context of attitude score, significant relationship was found with education level and socioeconomic status as shown in Table 5. Participants with higher level of education had a better attitude score (p=0.036), similarly those with better socioeconomic status had a better attitude as compared to those with low socioeconomic status (p=0.018).

A significant correlation was found between knowledge and practice score, which means that those with good knowledge of COVID-19 were more likely to follow good practices for preventing spread of COVID-19 where the coefficient of correlation was calculated to be 0.3 (r=0.3, p=0.002) as shown in Figure 3.

Table 5: Association of knowledge, attitude and practice scores with sociodemographic characteristics

Sociodemographic characters	Knowledge Score			P value
	Poor (<10)	Good (10-12)	Excellent (13-17)	
Gender • Male • Female	 5 (41.7%) 7 (58.3%)	 7 (25.9%) 20 (74.1%)	 25 (35.2%) 46 (64.8%)	0.564
Education level • Illiterate • Undergraduate • Graduate	 3 (25.0%) 7 (58.3%) 2 (16.7%)	 3 (11.1%) 20 (74.1%) 4 (14.8%)	 14 (19.7%) 44 (62.0%) 13 (18.3%)	0.771
Socioeconomic status • Low • Middle	 6 (50.0%) 6 (50.0%)	 13 (48.1%) 14 (51.9%)	 25 (35.2%) 46 (64.8%)	0.382
	Attitude Score			p
	Poor	Good	Excellent	
Gender • Male • Female	 2 (18.2%) 9 (81.8%)	 22 (30.6%) 50 (69.4%)	 13 (48.1%) 14 (51.9%)	0.133
Education level • Illiterate • Undergraduate • Graduate	 0 (0%) 8 (72.7%) 3 (27.3%)	 10 (13.9%) 50 (69.4%) 12 (16.7%)	 10 (37.0%) 13 (48.1%) 4 (14.8%)	0.036
Socioeconomic status • Low • Middle	 3 (27.3%) 8 (72.7%)	 24 (33.3%) 48 (66.7%)	 17 (63.0%) 10 (37.0%)	0.018

	Practice Score			p
	Poor	Good	Excellent	
Gender • Male • Female	 14 (46.7%) 16 (53.3%)	 23 (29.5%) 55 (70.5%)	 0 (0%) 2 (100.0%)	0.142
Education level • Illiterate • Undergraduate • Graduate	 5 (16.7%) 19 (63.3%) 6 (20.0%)	 14 (17.9%) 51 (65.4%) 13 (16.7%)	 1 (50.0%) 1 (50.0%) 0 (0%)	0.786
Socioeconomic status • Low • Middle	 15 (50.0%) 15 (50.0%)	 28 (35.9%) 50 (64.1%)	 1 (50.0%) 1 (50.0%)	0.391

Figure 1: Scores of knowledge, attitude and practices.

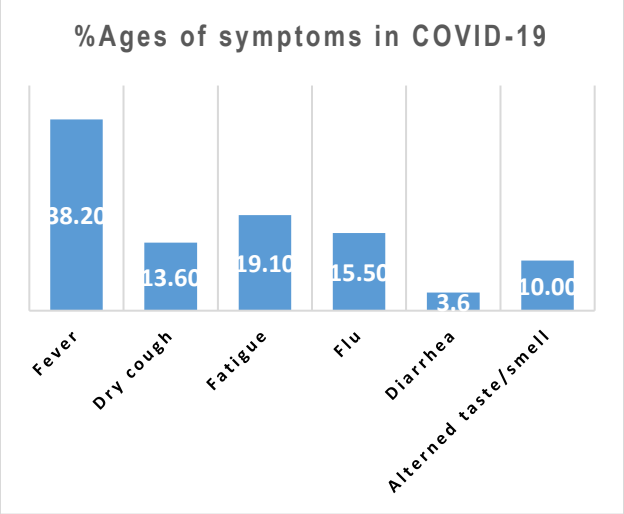

Figure 2: Awareness of COVID-19 symptoms reported by study participants (n=110).

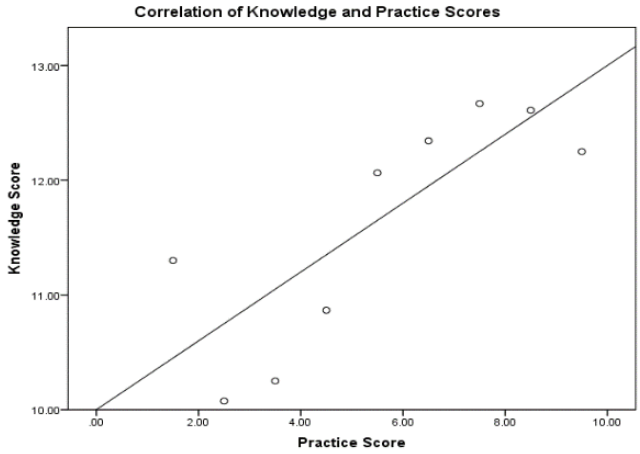

Figure 3: Relationship of knowledge and practice score.

Discussion

As clinicians, we know that the age-old adage of 'prevention is better than cure' will remain true for all times. Doctors can play a major role in spreading awareness about prevention of communicable diseases. Effective communications skills can ensure that patients get a fair idea about the disease and different measures to prevent its spread. Many studies [16] carried out during this pandemic showed that immunosuppressed patients and those patients suffering from rheumatologic diseases are more likely to get COVID-19 infection and more likely to succumb to its complications including death.[17] Therefore, it was important to get an idea about the beliefs of our rheumatologic patients regarding current pandemic and their attitude towards its prevention.

In our study we found that our patients had acceptable knowledge about the COVID-19 symptoms and preventive measures i.e., 64.5% had an excellent knowledge, 24.5% had good and 10.9% had poor knowledge. A similar survey done recently by Ladiwala et al. among Pakistani population showed that the study population had adequate knowledge about COVID-19 (93.3%) [18] which is parallel to the knowledge assessed in our study (89% - total of good and excellent knowledge). This is also in accordance with the results of a study done on rheumatic disease patients in Tanzania [19] and a similar one done in Nepal in 2020 in which >90% had knowledge about the route of transmission, clinical features and also preventive methods.[20]

It was noted that 48.2% of our sample thought that their rheumatic disease puts them at a higher risk for COVID-19 compared to 31.5% rheumatic disease patients in Nepal who knew they were at risk. On the contrary, a mere 1.8% of our study population while 18.9% of the Nepalese cohort thought that their medication predisposed them to develop the disease.

It was interesting to note that 20% of our patients did not believe in the existence of this pandemic and many of them considered it a propaganda. Of the people who believed in its presence, around one third (31%) of them believed there was no cure for the illness and once contracted it proves to be fatal. This belief definitely needs to be changed as this can lead to a feeling of doom in patients and might lead them to not seek medical attention when needed and thus avoid unnecessary morbidity and mortality. As for the domain of attitude in our study population, we found that in total 90% of the patients had good and excellent attitude regarding COVID-19 pandemic, similar findings i.e., 71% had a positive attitude towards COVID-19 in the Nepalese cohort.[20] Majority of the participants believed that the measures taken by the government were good enough to curtail the spread of the pandemic in Pakistan.

Practicing the preventive measures appropriately has been one way to stop the spread of the virus among the masses. It was noted that in our study population around 38 (34.5%) participants were still going to crowded places like mosques, markets, weddings etc. during lockdown. It was noted that even at the peak of third wave patients were still going to religious congregations clearly indicative of their religious inclination. Overall, one third of the study population was found to have good and excellent preventive practices. This observation is similar to statistics from other under developed countries like Ethiopia where poor practices were observed in 47.3% while 25.9% of study participants had good practice. Only 38.1 % of their study population avoided going to crowded places.[21] Statistics form developed countries show better scores for practices probably as a result of better literacy rate and understanding of ways through which the disease spreads. A study conducted in Netherland on 979 patients with rheumatic diseases compared to 414 healthy controls, found that patients with rheumatic diseases followed the isolation measures twice strictly compared to the healthy controls.[22]

This pandemic has certainly caused financial burden on people around the globe, our local population is no different in this regard. Almost two thirds of the patients (61%) responded that they have encountered decrease in their income. The COVID-19 Global Rheumatology Alliance Patient Experience Survey carried out in over 90 countries throughout the world, found that there was an increase in the unemployment, nearly one third of the 9300 total respondents had a decrease in full-time employment, which ultimately affected the financial status of the patients.[23]

This study did not show any strong association between socioeconomic background of patients and their KAP score but similar studies in USA,[24] Malaysia [25] and China [26] showed that the socioeconomic background of the patients did affect their KAP score, higher socioeconomic status of the population was associated with better knowledge and practices. The reason we did not find any association for this could be that the majority of the patients coming to the Rheumatology clinic belong to Islamabad or its suburbs. Being from the capital city and because of strict implementation of COVID-19 SOPs in this region, has perhaps led to better understanding of the patients towards the COVID-19 pandemic and has resulted in fewer number of affected patients in the city.

One other aspect that needs attention in particular is the impact of COVID-19 on the mental health of general population and in particular on patients with rheumatic diseases who are already in a lot of mental stress because of chronic nature of their disease and the morbidity

associated with it. Almost 53% of the patients in our study responded that they were experiencing mental stress because of this pandemic, a finding consistent with the result of a study done in Italy in patients with rheumatic diseases showed that 44.2 % patients had shown some worsening in their mental wellbeing ever since the pandemic began.[27] Similar findings were observed in India where 64% of the rheumatic disease patients had some degree of mental stress.[28]

At the time that this survey was being conducted, there was intense research going on in the world regarding development of effective vaccine against COVID-19 virus. Even though the long-term effects of vaccine are yet to be seen, as of now, it is strongly emphasized that people from all walks of life get themselves vaccinated. Our study clearly indicated that patient's attitude towards vaccination needed to be changed. Only less than half (46%) of the patients said that given the option for vaccination they would consider it. It is important to note, however, that this survey was conducted when vaccination facility had not been opened for general public and only frontline workers were being vaccinated so understandably there was some reservation on part of patients. It needs to be seen whether this attitude changes once mass vaccination is opened.

Conclusion

Overall, it was noted that KAP of our local rheumatologic patients towards COVID-19 infection was reasonable, however, it must be kept in mind that this was primarily carried out in an urban population and hence, results might not be representative of the opinions of rural population. Hence, more studies need to be carried out to get a clearer picture. The devastating effects that the third wave of this pandemic has had in our neighboring country India, clearly shows that we still need to keep our guards high and at no cost should we neglect the laid down SOPs for the disease.

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ORIGINAL ARTICLE

The correlation and determinants of cost-benefit analysis of measles vaccines among the medical centers providing Expanded Program on Immunization (EPI)

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Author`s Contribution

[1] Conceptualization analysis and investigation,
[2] Data analysis, data collection
[3] Write up
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A B S T R A C T

Introduction: Measles is a highly contagious viral infection, vaccine-preventable diseases claim the lives of nearly 30 million people each year around the world, including 17% of children under the age of 5.

Methodology: This was a descriptive and cross-sectional investigation. Retrospective data collection was used. We looked at medical centers that provided EPI administrations.

Results: Around 8% of the youngsters in the study were found to have measles, according to the health center's records. There are an undetermined number of measles-infected children. Only 12% of those surveyed had received the measles vaccine, and the vast majority (88%) had never received the shot. According to statistical analysis, the study's r square value is r=0.35, which is considered to be an intermediate direct relationship (Wastage of vaccine and total cost). It illustrates that if there is no system of checks and balances on vaccine waste, it could have an impact on the overall cost of the vaccination. Vaccines wastage shows a positive association with Dose wastage x2= 438.8 (p-value 0.002). the breakage of vaccine vial x2 = 369.6 (p-value 0.015), expiration of vaccines x2 = 1068 (p-value 0.006), cold chain maintenance x2 = 79.99 (p-value 0.014) & inventory missing was x2 646.9 (p-value 0.004) showed statistical significance.

Conclusion: The elimination of any disease would be contributed by the parallel factors one of that includes also financial state. In less time and cost we can vaccinate the number of children and can achieve universal coverage of immunization.

Keywords: *Cost effectiveness, epidemiology, measles, public health, vaccine*

Introduction

When someone has measles, it spreads quickly from them to others. Children are especially vulnerable because of their lower levels of immunity, and the most common complications associated with measles include encephalitis, diarrhea, an inability to eat, pneumonia, and otitis media. Fever and severe rashes all over the body are the main symptoms, and the sufferer can spread the virus to others.[1] The world is following sustainable developmental goals in 2030 to achieve maximum health. Although the evolution of vaccination in the early years of life helped a lot in the reduction of global mortality and morbidities still many regions of the world are devoid of these due to multiple reasons. So far we have been able to eradicate only one disease that is small pox, for the total elimination of these diseases it needs a very systematic plan and implementation of all SOP's.[2] Well educated and dedicated working staff, procurement of vaccines, maintenance of sera's and vaccines such as cold chain instruments, transportation and delivery system, logistics, usage of vaccines proper disposal of

syringes, correct data recording, awareness of the community, regional, religious and political support, constant monitoring and evaluation these are the factors which when all work simultaneously can give the hope of eradication of the diseases globally.[3] Vaccines are one of the best wellbeing mediations that realize huge decreases in irresistible infections weight load.

Vaccination of children against early life tuberculosis, poliomyelitis, diphtheria, pertussis, tetanus and measles is also helping to reduce mortality and morbidity in Pakistan since 1978, not only vaccination of this disease and also a number of new vaccines such as hepatitis B, Hib and pneumococcal vaccine (PCV10) were introduced. These vaccines including Hemophilus influenza type b, 88 percent of the Punjab province's population have been immunized, making it possible to eradicate maternal and neonatal tetanus and other tetanus-causing diseases in 2016.[4] It has been estimated that in Vietnam 26,000 deaths & 5.7 million diseases cases were prevented by the active and prompt working of EPI, $1000 to 27000$ cost-effectiveness were recorded on the preclusion of per death.[5]

Elimination or reduction in the measles outbreak will need a lot of focuses on the improvement of surveillance, handsome amount to the workers, maintenance of cold chain or the suitable medium for vaccination, community awareness campaigns and advocacy of the people, availability of vaccines at the health facility, this strategy may increase the coverage rate up to 60 % to 90%.[6] Immunization and vaccination programs are necessary for the elimination and eradication of measles from any region, for achieving this target more than 95 % vaccines (MCV1 & MCV2) coverage should be there.[7]

In several aspects, immunization is a unique form of human services mediation. Vaccines serve as a preventative measure and are typically given to healthy individuals when they are young. However can cause a (little) danger of genuine unfriendly impacts in immunization beneficiaries. In a perfect world, immunization projects are taken off with a long haul, population wide, general wellbeing objective as a top priority, considering the regularly generous for the most part positive and defensive roundabout impacts in unvaccinated gatherings (for instance, neonates, people with stifled resistant frameworks, and the older) by method for decreased course of preventable pathogens in the more extensive populace.[8] The more prominent effect of triggered campaign in low-inclusion circumstances is to a great extent the aftereffect of progressively visit triggered campaign. In the Yemen-like circumstance, a touchy serologic trigger (i.e., 10% weakness in kids) prompts TCs being led in 10 out of the initial 15 y from arrangement execution, basically turning into a normal occasion.[9] Use of internet of things also paying their part, eHealth is prevailing almost all over the world, mobile and smart phones innovation would be much helpful in the registration of care givers and vaccination receiver's hence the surveillance can be achieved; a little cost at an initial point can prevent huge loss afterward. The 78% of coverage has been analyzed by using a direct phone call in immunization campaigns.[10] This policy of using technology is not even feasible but also less time consuming, identification of the next child and its next dose and also creating awareness among the low literate communities.[11,12]

It's a dilemma that day by day public health finances are reducing in developing countries due to other political priorities. Any public health policy developed for the promotion of health will surely work such as the vaccination at early stages of life, early diagnosis and prompt treatment, immunization programs have reduced 60 % and more mortalities at child hood life.[10] Public awareness program have a significant impact on the community's sociological and behavioral health, a study gave the results of more than 50 % of population tends to immunize their kids in order to avoid measles after the electronic and social media campaigns.[13,14] The evidence shows that professional birth attendants have a significant role in the measles immunization as it is 1.5 times more likely to vaccinate as the children being birth by the unprofessional birth attendants or health care providers (OR = 1.49, 95% CI: 1.43–1.56).[15]

World health organization and other global health agencies are more focusing on immunization/ vaccination and aimed to reduce the mortalities and morbidities for the achievement of sustainable development goals, despite such efforts and expenses in African region it has been estimated that 28000 deaths occurred annually due to measles.[16] The issue arises mainly due to the least coverage by the unstable and weak immunization

programs and health system of most of the low and middle-income countries. The two-dose schedule is not following by all the health systems and thus collapsing the aim of health for all.[16,17]

In 2013 all the six regions of world health organization collectively decide to work on the elimination of measles by 2020. Multiple strategies & policies were launched, such as for appropriate surveillance and accurate diagnosis of disease Global Measles and Rubella Laboratory Network (GMRLN) were created. GMRLN is developing constantly and in January 2017 it has 703 labs working in 191 countries. It also ensures the quality control and quality assurance for the consistent methods and operations, validities and accuracies, provision of best quality results and training.[18] In spite of these chronicled triumphs, immunization isn't only a story from an earlier time. Stanley listed twenty-two ailments and diseases for which powerful vaccines exist yet in addition forty-seven others for which adequately compelling immunizations are not accessible.[19]

A total of seven Infectious illnesses, a considerable lot of which are preventable, stay a main source of overall mortality. For example, around 6.3 million kids more youthful than age five bite the dust every year, and about portion of these passings are the aftereffect of pneumonia (frequently brought about by flu or pneumococcus); loose bowels (regularly brought about by rotavirus); or different illnesses brought about by conceivably immunization preventable contaminations, for example, measles, lockjaw, tuberculosis, and intestinal sickness.[20] Environmental change modifies conditions and enables creatures to thrive in beforehand unfriendly situations. Populations are increasingly versatile, and globalization and expanded urbanization consider more noteworthy development of individuals and microorganisms, along these lines adding to sickness transmission.[21]

The well economical and financial condition of any family has a great effect on the immunization coverage as parallel with financial status educational and attitude towards disease and prevention is also lower as compare to developed and educated population, a study from less developed area shows that more than 40 % of children were not fully immunized (95% CI (0.083-0.077) and 78 % were uneducated mothers were there among unimmunized children. [22,11] Another study also supports the determinants of education and financial condition in the unequal immunization of the measles among children, education and knowledge about disease occurrence, treatment and prevention (AOR = 0.02, 95% CI: 0.001, 0.68) and low socio economic condition also have a negative effect on vaccination (AOR = 0.15, 95% CI: 0.1, 0.43).[13,16] The study's goals include ensuring equal access to health care for all people, regardless of their socioeconomic status. Individuals will receive low-cost medicine, including vaccines. The study's objective include identification of the cost variables and addressing the issues such as measles outbreaks, and to evaluate the factors that can speed up the immunization process after lowering the cost.

Methodology

The study was done at the capital territory area of Islamabad. The duration of the study was 3 months. The primary source of information was the Islamabad extended immunization program. Regulating and coordinating the National Health Services Ministry Islamabad. It comprises all children under the age of five in the locality (rural and urban) Descriptive and cross-sectional research methods were employed during the examination We looked at medical centers that gave EPI administrations and found a few that did. Misuse of vaccine usage structures, resistance development registers, and month-to-month EPI reports provided information on immunization use. For vaccine and consumable costs, UNICEF-WHO value projections were used. Unit costs for auto incapacitate, weakening and security boxes were also used to estimate vaccine and consumable costs. A variety of expenditures (such as labor, transportation and EPI running) were acquired through meetings and direct surface estimations of structures as well as the abuse of various records (such as vaccination sessions plans, count sheets, staff pay vouchers and receipts and building gathering archives) in addition to support for virus chain running, amortization for structures and 'moving stock' and iceboxes.

The cold chain at EPI was fully exploited for the program. Staff expenses were calculated by multiplying their compensation by the amount of time they spent on EPI trainings and then adding any extra compensation they received during that time period. Inoculation

sessions, vaccine transportation, disclosing (vaccination and disease observation), coordination gatherings, supervision, and cold chain temperature checking and maintenance are among the activities under consideration. In order to analyze the data and information, Excel programmers used a spreadsheet created for the purpose of information aggregation.

The number of fully immunized youngsters was the primary indicator of success (children who got dosages of measles). The expenses of the region health facility administration were shared to the facility focuses by procedure in extent to target populace secured. The different markers utilized were the normal expense per portion utilized (all out costs/complete dosages utilized) and the normal expense per portion regulated (absolute costs/all out dosages managed - the stuff to direct a portion. Null hypothesis shows there is no standard correlation between Wastage of vaccine and total cost of vaccine while Alternative hypothesis shows there is significant standard correlation between two variables that are wastage of vaccine and total cost of vaccine.

The ethical consideration and consent was taken from the educational institute (Hamdard University Islamabad), Official consent from the authorization EPI, Ministry of health, different health care facilities were taken. Data will be used only for the intention of research and data analysis. The confidentiality and inscrutability of participants should be secured. Regression analysis was done and for vaccine production and chi-square was applied for the association of vaccine wastage with other factors & p-values was analyzed.

Results

Frequency of vaccinated and no vaccinated children:

Around 8% of the youngsters in the study were found to have measles, according to the health center's records. The number of measles-infected youngsters that are unidentified was unknown. Only 12% of those surveyed had proof of receiving the measles vaccine, and the vast majority (88%) had never had the shot as shown in Figure 1.

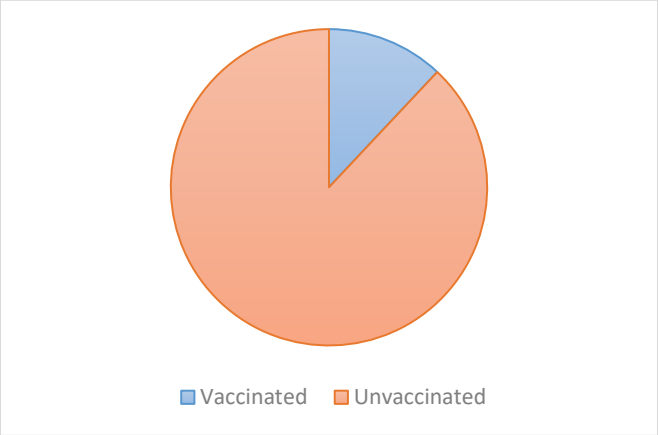

Figure 1: Percentage of vaccinated children present in the study

Significance of the study:

The analysis of results shows that the p value is (0.002) that is less than our alpha α value that is 0.05. The p-value, on the other hand, reveals the results that are statistically significant, such as ours (p-value 0.002) at a 95% confidence level as shown in Table 1.

Table 1: Significance of the study at 5 % level

	Intercept	
Coefficients	103.3791	2.661327
Standard Error	54.78353	1.086844
t -Stat	1.887046	2.448674
P-value	0.002839	0.002381

Table 2: Upper & lower values at 95% confidence interval

	Intercept	
Coefficients	103.379	2.66133
Standard Error	54.7835	1.08684
t -value	1.88705	2.44867
P-value	0.00284	0.00238
Lower 95%	9.94931	0.41302
Upper95%	216.707	4.90964

Correlation analysis:

The statistical analysis of results have shown that the r square value of the study r = 0.35 fall in the intermediate

direct relation category between the variables (wastage & total cost of vaccine). It has shown that there was a positive correlation between wastage of vaccine and the total cost charge of vaccine as shown in Table 3 and 4.

Table 3: Correlation analysis of vaccine wastage and total cost of

Regression Statistics	
Multiple R	0.454
R Square	0.356
Adjusted R square	0.172
Standard Error	59.78

Table 4: Cost applied on various important variables used in preparation and final shape of measles vaccine

Variables	Purchasing price rupees
Vaccine concentrate	20 – 25
Material used in preparation	08 – 10
Electricity consumption	12 – 15
Transport / fuel charges	15 – 18
Packaging	05 – 08
Cold chain	20 – 28
Salaries of workers	50 – 60
Total	150 – 170

The variable cost shows that if we reduce the electricity bills, we can decrease our purchase values if we shifted this electricity consumption to solar panels that are much cheaper than the electricity per unit which is one of the most important factors. By reducing the expenses, the coverage of immunization may be increase toward the universal or 80 % to 90%. This value will help in the long after effects in the economics and social status of individual as well as the state or country level, which eventually make the nation prosper and developed.

Association of vaccine's wastage with the different factors:

Table 2 reported the associations of dependent variables with outcome of interest i.e. vaccines wastage. Using Chi-square test, vaccines wastage showed a positive association with Dose wastage x^2= 438.8 (p-value 0.002). Breakage of vaccine vial x^2 = 369.6 (p-value 0.015), expiration of vaccines x^2 = 1068 (p-value 0.006), cold chain maintenance x^2 = 79.99 (p-value 0.014) & inventory missing was x^2 646.9 (p-value 0.004) showed statistically significant relationship with cost effectiveness of vaccine wastage. Statistical analysis showed that vaccine's wastage and trained & skillful staff were strongly associated x^2 462.5 (p-<0.05). The analysis also revealed that open vial wastage of vaccines was more prevalent (21%) than the vials which whole dose was administrated (27.8%). The results were given in Table 5 below.

Table 5: Association of vaccines wastage with other factors

	Vaccine wastage			
Variable Category	Yes= 43 %	No=57 %	X^2	p value
Dose wastage			438.8	0.002
< than 2 dose per 10 doses	31	00		
> than 2 dose per 10 doses	12	00		
Breakage of vial			369.6	0.015
> than 20 vial per 100 vials	9	00		
< than 20 vial per 100 vials	34	00		
Expiry of vaccine			1068	0.006
Yes	20	02		
No	23	55		
Cold chain maintenance			79.99	0.014
Yes	10	57		
No	33	00		
Trained & skillful Staff			462.5	0.036
trained	34	49		
Untrained	09	08		
Open vial wastage			388.9	0.001
Yes	21	04		
No	22	53		
Missing of inventory			646.9	0.004
Yes	15	06		
No	28	51		

Discussion

Elimination of any disease could be contributed by the parallel factors one of that includes also financial state. In less time and low cost, we can vaccinate the more number of children and can achieve herd coverage of immunization. Under vaccination remains dilemma to worldwide that a huge number of

children are devoid of vaccination and being neglected by the immunization programs.

There were 2058 (30%) kids unvaccinated and 4889 (70%) inoculated for measles. Among those detailing inoculation, 773 (16%) detailed by means of dated card, 3990 (82%) through maternal review, and 126 (3%) by means of stamped card. In our study it also shows that just 12% of the children were vaccinated rest of them never immunized with measles vaccine. Whenever uncovered, 90% of unvaccinated explorers without other proof of measles invulnerability become sick with measles. This hazard is diminished to 7% among uncovered voyagers with 1 MMR immunization and 3% among explorers with 2 MMR inoculations.[2,23,24] In a setting with high gauge inoculation inclusion levels, SMS updates combined with motivators altogether improved vaccination inclusion and practicality.

Given that worldwide vaccination inclusion levels have stagnated around 85%, the utilization of impetuses may be one choice to arrive at the staying 15%. Routine child immunization is one of the best and practicality general wellbeing mediations that have extensively decreased worldwide youngster grimness and mortality.[2,25] The impact of positive surrounding on the extent of youngsters with DPT3 was an expansion of 12.4 rate focuses contrasted with control (95% CI: 3.9 to 21.0, p=0.005), contrasted and an increment of 16.7 rate focuses (95% CI: 8.2 to 25.2, p<0.001) when the data was contrarily encircled.[24] Be that as it may, there was no distinction when the 2 data gatherings were contrasted and one another (95% CI:−5 to 13, p=0.352). Looking over all the auxiliary results, the surrounding of data had no impact, except for information of avoidance. Results remained subjectively a similar when we balanced appraisals with the incorporation of covariates and when utilized a Bonferroni amendment to manage the issue of different theory testing.[26]

In any case, every year, an expected 18·7 million kids under 1 year of age don't get fundamental inoculation as a component of an extended program of vaccination (EPI) around the world, and a huge number of kids kick the bucket from immunization preventable sicknesses.[27,28] Due to social issues and inadequate gratefulness for vaccination, guardians and parental figures overlook or disregard the significance of inoculation or finishing the whole arrangement of antibodies. As an outcome, there is a continuation of the polio plague, huge measles episodes, and high illness weight of antibody preventable infections in children. Discoveries from a pilot study evaluating the beneficial vaccination inclusion utilizing SMS content and robotized calls demonstrated an a lot higher reaction to the computerized call (78%) than SMS instant messages (3%; individual correspondence).[29,30]

Childhood immunization still stays one of the savviest preventive procedures against mortality and dreariness among kids. Vaccination spares the lives of up to 3,000,000 kids, each year. High paces of antibody inclusion could avoid an extra 1.6 million deaths a year among kids younger than five. The objective of the national EPI is to guarantee full immunization of children against preventable maladies.

EPI is a standard action inside the open social insurance framework. What's more, time explicit mass inoculation battles and entryway to-entryway exercises are consistently actualized the nation over to help increment routine inoculation take-up [30] Vaccine production's cost effectiveness can be achieved by adopting E-health various mechanisms. By subsidizing various vaccines and go towards direct recruitment regardless of tenders so only good quality products can be acquired. By addressing those determinants which are very much contributing towards cost as mentioned in results in Table 1, the multi dose vaccine to make it more affordable and also increasing the efficiency. Electricity is a major factor in cost increasing while switching of electricity to solar panel and systems can help in cost effectiveness.[1]

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REVIEW ARTICLE

Role of defensins in innate immunity

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[3] Supervised and final review

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A B S T R A C T

Immune system of living organisms ranging from fungi, plants, vertebrates and invertebrates are all aided by polypeptide chains like defensins and cathelicidins. In humans the defensisns are quite fundamental part of innate immune system in combating with day-to-day exposure to unknown pathogens. The defensins are classified as alpha beta and sigma defensins expressed at chromosome 8 at nearly same positions, the sigma defensin is however synthetically developed as reterocyclin, as it has been stopped producing because of evolutionary development of stop codon 7.5 million years ago. The expression of Defensins can be either constitutive or inducible through epithelial cells, Paneth cells or other respective immune cells to regulate the activation of the innate immune responses. These impart their role either by direct microbicidal action, antiviral activity, inactivation or neutralization of microbial products, mobilization or activation of phagocytes and mast cells. Further to this there is lot more to explore about the availability of similar genetic expressions as defensins with unclear functions and *in vivo* experimental models development.

Keywords: *Anti-microbial polypeptides, defensins, Innate immunity, Toll like receptors TLRs activation*

Introduction

The polypeptides chain responsible for supporting immune system is quite old phenomenon, the poly peptides in mammals that take part include defensins, cathelicidins and others.[1] The defensins are quite broad spread in living organisms ranging from insects, fungi, plant, invertebrates and vertebrates. As Humans are vulnerable to many unknown pathogens, the defensins help in an effective immune response against such, disease causing agents. Defensins are classified as positively charged cysteine containing host defense polypeptides originating from either epithelial cells or neutrophils, performing multiple functions along with efficient role in innate and adaptive immune response against foreign microbes and pathogens. Initially defensins were discovery as; alpha defensins (α) from rabbit neutrophils in 1985, subsequently beta defensins β were discovered (1990) in a bovine of mouse and in human intestinal epithelium.[2]

Classification of Defensins:

These were classified as per presence in mammals as α, β and θ defensins. These molecules have amphiphilic structure with much conserved region of six cysteine molecules and di sulfide bonds but still vary in structure, origin and function.

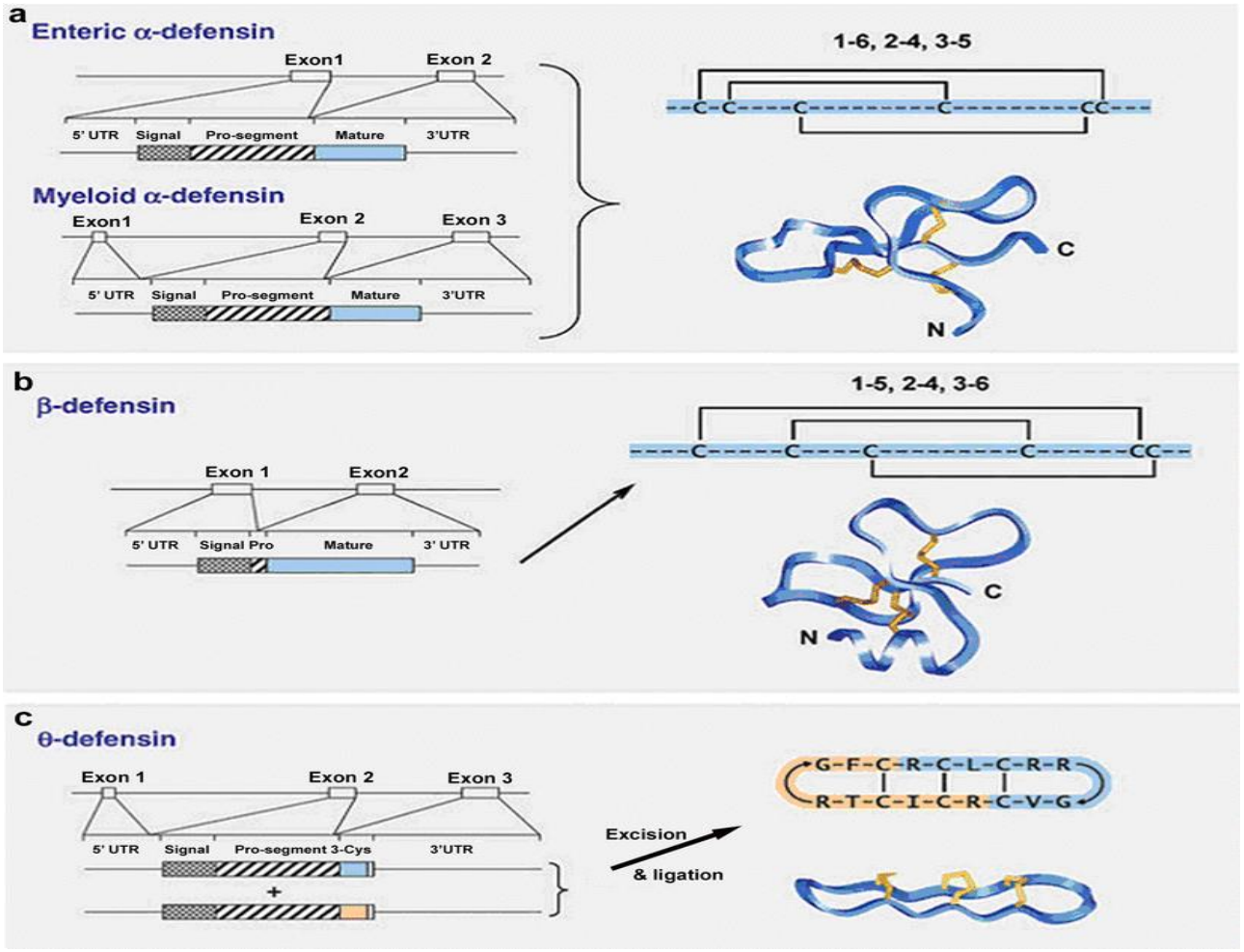

Figure 1: **Defensin genes and peptides** [22]

Alpha defensins:

In humans these defensins originate from neutrophils and epithelial cells. The first four have been studied and extracted from neutrophils in humans are (HNP1~4) as shown in Figure 1, while the other two were found in Paneth cells present in intestinal epithelial called as human defensins HD5 and HD6 or enteric defensins.[3,4] The cysteine disulphide bonds are between the 1-6, 2-4, 3-5 cysteine residues [5,6] and have 29 to 35 amino acid sequence.[7]

Beta defensins:

In humans these are composed of more than 36 amino acid residues and are found in epithelial tissues mostly, so far 28 genes for beta defensins have been discovered but only Human Beta defensin (HBD1~6) and HBD 2, 3 are studied extensively.[8] While the cysteine links are at the connections are 1-5, 2-4, 3-6 forming disulphide bridges, these bonds not only add positive charge but also add stability to structure.[9]

Sigma defensins:

In humans the development of sigma defensin have silenced because of an evolutionary development of a stop codon 7.5 million year ago [10] however, this have been developed synthetically as reterocyclin.[9] It has a circular hair pin structure with cysteine di sulfide bonds between 1-6, 2-5, 3-4 residues.

Genetic Expression of Defensins:

The human defensins alpha and beta specifically are expressed at nearly same location at Chromosome 8, there loci and genetic expression along with their cellular expression, role in immunity and concentration in diseased condition is mentioned in Table 1. In this no genetic expression is mentioned for HNP (Natural human

neutrophil defensin) HNP2 it is thought that HNP1 and /or HNP3 genetic expressions might have gone by a proteolytic activity to express HNP2. [11]

Defensins Synthesis and regulation & release:

Defensins are synthesized and released when the host body is exposed to a pathogen, the immune system in response to that produce these polypeptides either from epithelial cells or from neutrophils. Their expression could be constitutive or inducible i.e., in response to chemical mediators or other cells or in response to pathogenic exposure respectively. The cytokines or the mediators for development and release of the defensins are mentioned in Table 1. Defensins are expressed whenever the host immune cells get exposed to pathogenic content, as in case of toll like receptors (TLRs) activation. TLRs 1,2,4,5.6 and 8 are present on the surface of immune cells and some of the epithelial cells while TLR 3, 7 and 9 lies on the endosomes of the immune cells.

When the TLR 1 /2 complex gets activated by exposure to microbes with the help of its adaptor proteins MYD88/ TRAF6 it activates the kinases pathways ultimately activating NFkB that enters into the nucleus of cell and generate the transcription of required proteins and this case defensins and cytokines production that ultimately leads to the pro or anti-inflammatory responses. Similarly, the activation of TLR5 and 4 the transmembrane receptors activate MAPK pathways along with JNK and p38 pathways that ultimately end up in generation of cytokines and chemokines that act as precursors for defensin release and immune response generation. The anti and the pro inflammatory processes are well summarized in above schematic Figure 2.

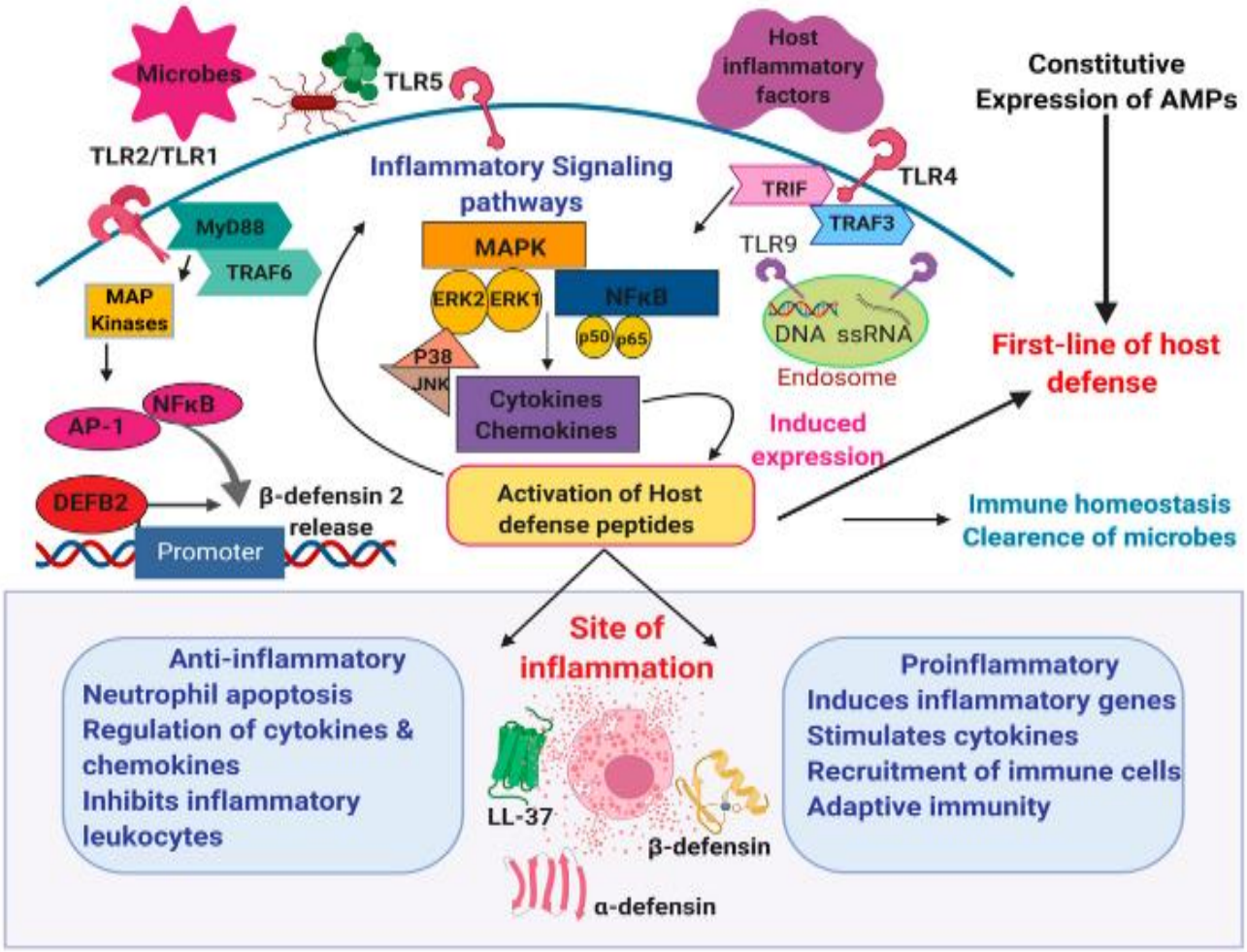

Figure 2: Expression of defensins in immunity [12]

Table 1: Cell sources and regulation of mammalian defensins [12]

Defensin				
Conventional name	Type	Cell source	Synthesis	Release
HNP1 ~ 4	α	Neutrophils CD8 T cells	Constitutive Inducible	Degranulation Secretion?
HD5 ~ 6	α	Paneth cells	Constitutive	Degranulation
Mouse cryptidin	α	Paneth cells	Constitutive	Degranulation
HBD1	β	Keratinocytes and epithelial cells	Constitutive and inducible	Secretion
HBD2 ~ 4	β	Keratinocytes and epithelial cells	Inducible	Secretion
BNDBs	β	Neutrophils	Constitutive	Degranulation
Bovine TAP	β	Epithelial cells	Inducible	Secretion
RTD-1	θ	Neutrophils, monocytes	Constitutive	Degranulation
Cathelicidins		Neutrophils, keratinocytes, epithelial cells, mast cells, and monocytes/macrophages	Constitutive and inducible	Degranulation or secretion
EDN		Eosinophils, neutrophils, macrophages, and placental epithelial cells	Constitutive and inducible	Degranulation or secretion

*Abbreviations: EDN, eosinophil-derived neurotoxin; HNP, human neutrophil peptide; HD, human defensin; HBD, human β-defensin; BNDB, bovine neutrophil-derived β-defensin; TAP, tracheal antimicrobial peptide; RTD-1, rhesus theta defensin-1.

Role in Innate Immunity:

- **Direct microbicidal action:**

The direct microbicidal action against bacteria is documented by alpha defensins and they perform it by detecting a more negatively charged cell membrane and forming a pore in it with a dimeric alignment of alpha defensins. This pore makes the internal constituents exposed to external environment and cell death. HNP1, 2, 3 and 4 along with HBD1 and HBD2 are found efficient in killing most of the gram positive, gram negative, fungi and few of parasites.[9] However, sigma defensin have shown this property in limited in vitro where salt and protein concentrations were found to be hindering their action in schematic Figure 3.

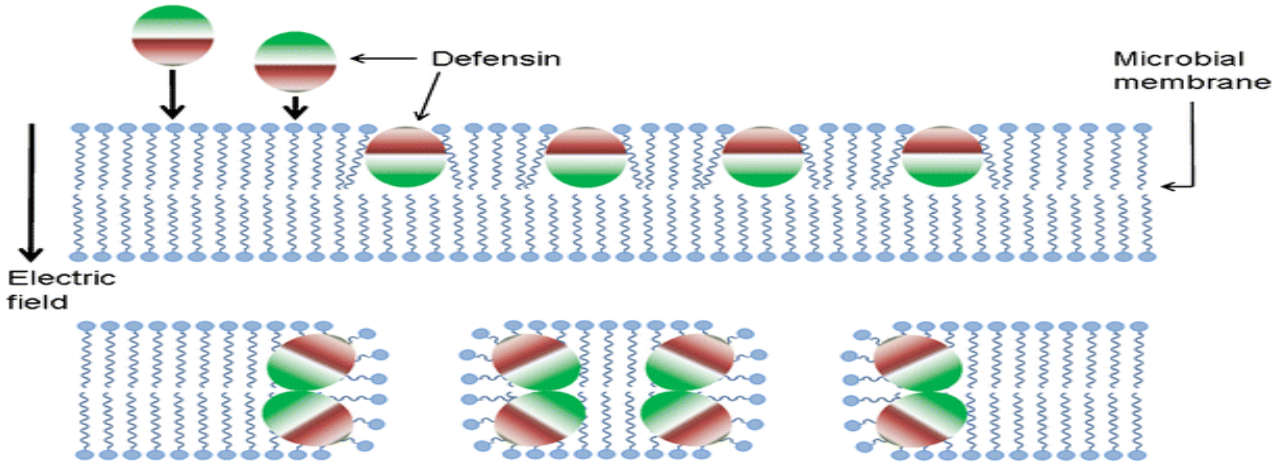

Figure 3: Direct microbicidal action against bacteria documented by alpha defensins [13]

- **Antiviral Activity:**

Antiviral activity of alpha defensins has been discovered a time ago but the antiviral activity has two aspects one is inhibition of viral invasion and the other is promotion of viral entry into host cells. For example, in case of HIV1 virus activity of HNP1-3 have shown non chemokine response. As these are capable of either direct viral inactivation or inhibition of adhesive and binding proteins gp120 and gp41 respectively on viral envelop, or the next step of viral fusion with cell membrane by down regulation co receptor CXCR4, direct membrane fusion of non-enveloped viruses like human papilloma virus are also inhibited by HNP1-3 and further viral RNA import and transcription is also inhibited, these features are quite promising in terms of viral prevention to prosecute infection in human cells but on contrary to that HNP 1 and Hd5 and 6 enhances a viral adhesion to epithelial cells and their entrance through tight junctions of trans epithelial cells. Thus, having quite, a contradictory and debatable effect against viruses in Figure 4.[14] "Opposing effects of human α-defensins on Inhibiting HIV-1 infection. (1) direct in activation of the virus (2) blockade of gp120-CD4 interactions (3) coreceptor downregulation, (4) Inhibition of gp41- and Env-mediated viral fusion (5) inhibition of nuclear import of viral RNA, (6) suppression of HIV transcription. Infection promoting mechanisms include: (7) enhancing viral adhesion/attachment, (8, 9) disrupting tight junction to promote trans-epithelial transmission of HIV"[14]

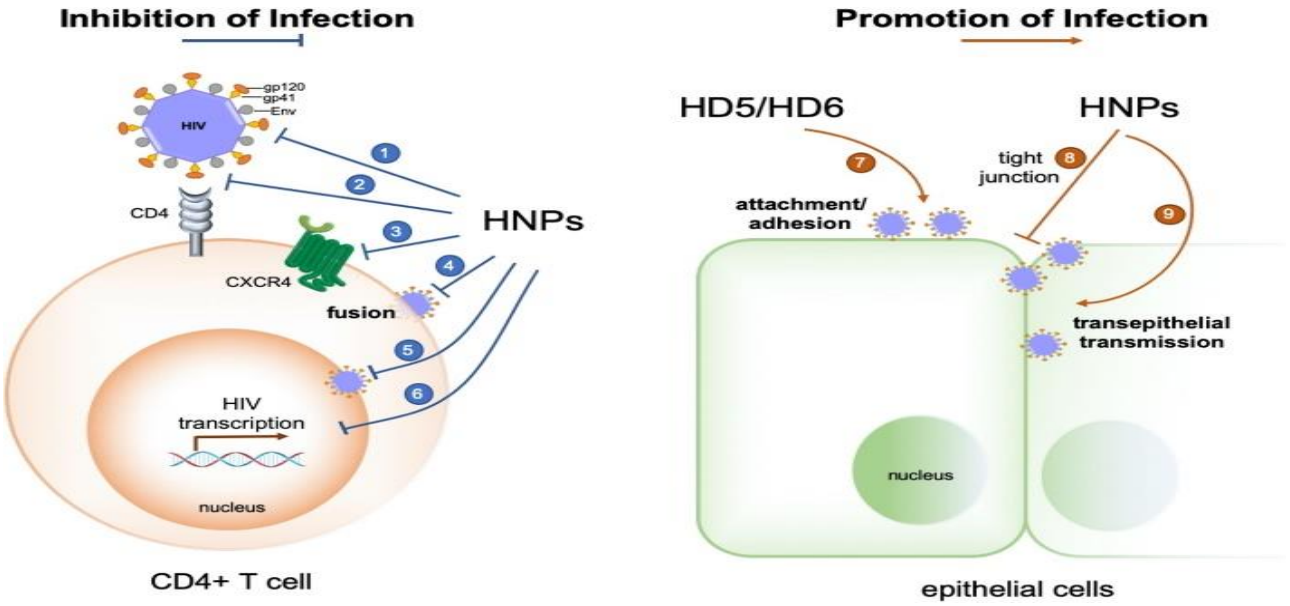

Figure 4: Direct viral inactivation or inhibition of adhesive and binding proteins gp120 and gp41 respectively on viral envelop [14]

- **Inactivation or neutralization of microbial products:**

Activity of HNP1-3 and θ defensins have been documented in mice against the lethal toxin of Bacillus anthracis it is a substrate-specific zinc-metalloprotease that can disrupt intracellular signaling making the cells weak and allowing the entry of bacteria unchecked. The alpha and sigma defensins have the ability to neutralize this exotoxin and the later also prevent the further germination of anthracs in host.[15] Moreover, HNP1, HNP 2 and BD2, 3 have recently shown binding activity with bacterial LPS [16] preventing its cytokine production through macrophage activation and preventing the LPS induced gene activation involved in sepsis, thus preventing this in mice.[17]

- **Mobilization and activation of phagocytes and mast cells:**

In innate immunity phagocytic activity of immune cells plays a very important role and for this the cells need to move out by four step mechanism including; rolling on endothelial surface, adhesion by cytokine receptors, diapedesis through chemotactic effect and migration to site of action as shown in Figure 5

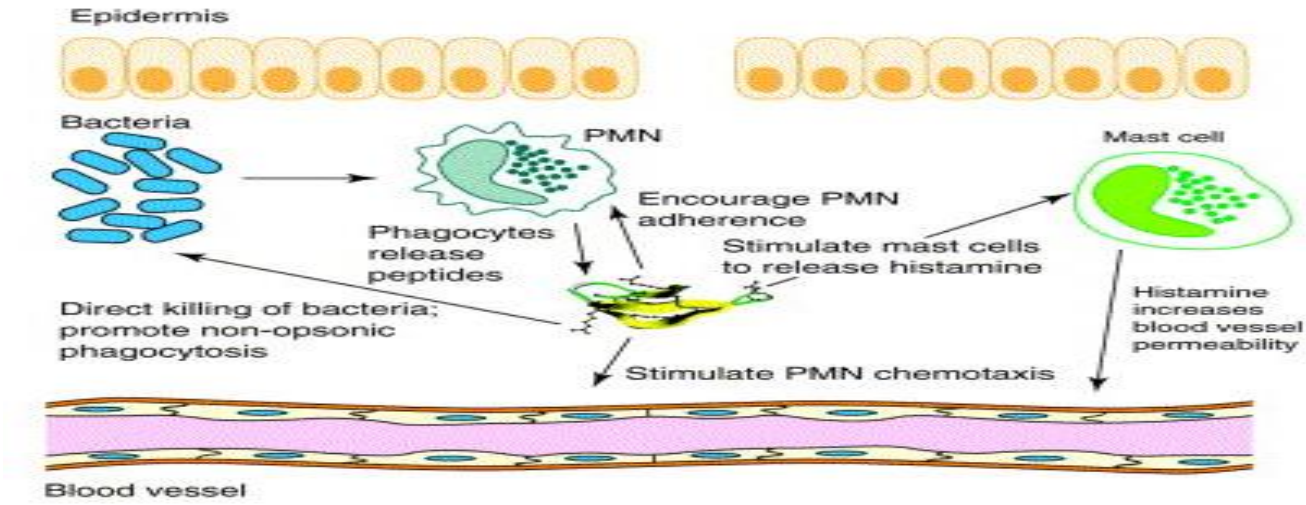

Figure 5: Mobilization and activation of phagocytes and mast cells in innate immunity [21]

- **Mast Cell activation and degranulation through defensins[18]**

The alpha defensins HNP 1- 3 and beta defensins HBD 3 and 4 act as chemoattractant for monocytes and macrophages.[18] HBD2 not only act as chemoattractant but has the ability to activate mast cells and thus production of inflammatory mediator prostaglandin D2. HNP1-3 and HBD 2 & 4 are not only involved as a chemotactic property but also increase the expression of production of cytokines receptors for strong binding of phagocytic cells and thus efficient migration to the site of action.[19]

Table 2: Multiple biological activities of mammalian defensins

Biological Activity		α-Defensin	β-Defensin	θ-Defensin
Microbicidal activity		All	All	All
Antiviral activity		HNP1, 2, 3, 4, HD5, RMAD	HBD1, 2, 3,	All
Exotoxin-inactivating activity		HNP1~3	ND	RTD
Endotoxin-neutralizing activity		HNP1, HNP2	HBD23	ND
Chemotactic activity	Mast cell	ND	HBD2	ND
	Mo/Mϕ	HNP1~3	HBD3, 4	ND
	DC	HNP1, HNP2	HBD1, 2, 3, mBD2, 3, mBD29	ND
	T cell	HNP1, HNP2, HNP4	HBD1, 2, 3	ND
Cell-activating activity	Epithelial cell	HNP1~3	HBD2, 3, 4	ND
	Mast cell	ND	HBD2	ND
	Mo/Mϕ	HNP1~3	ND	ND
	DC	ND	HBD3, mBD2	ND
Adjuvant activity		HNP1~3	HBD1, 2, mBD2, 3	ND

Abbreviations used: Mo/Mϕ, monocyte/macrophage; HNP1~3, a mixture of human neutraphil peptide 1~3; RMAD, rhesus monkey myeloid α-defensin; ND, not documented; HBD, human β-defensin; mBD, mouse β-defensin; RTD, retrocyclin (a synthetic artificial human θ-defensin).

Conclusion

Although it has been evident that defensins have been playing an integral role in immune response against pathogens but still there are some unanswered questions about multiple genomes found that appear like defensins but the role is unclear [20], further the activation and production of cytokines. And cytokine and defensin meditated immune cells activation is quite overlapping phenomenon that needs to be opened up in detail. In addition to this complete knock out models for defensins are still not present for finding out all the intracellular and molecular pathways, all the work done so far in *in vitro* or *ex vivo*, which is limiting factor in further molecular research.

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REVIEW ARTICLE

Spike protein of SARS-COV-2 as a potential target for phytochemical constituents: A literature review

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A B S T R A C T

SARS-CoV-2 belongs to well-known SARS Coronaviridae family. One of the main structural proteins of SARS-CoV-2 is the spike protein that is present around the surface of a viral cell and plays an essential role in viral attachment, fusion and invasion in host cell. Once a virus invades a cell, it replicates and infects other cells. The fundamental role of spike protein in the progression of viral infection has led to an increased interest in exploring agents that target the viral spike protein for effective control of CoVID-19. The related data from published articles reviewed and numerous phytochemicals that reportedly target the spike proteins of coronaviruses by computational studies briefly discussed. These active constituents possess the potential to develop as therapeutic and antiviral agents against SARS-CoV-2.

Keywords: *Phytochemical Spike protein, potential target, SARS-COV-2*

Introduction

The coronaviruses have been known since the 20th Century, viruses of this family have previously been identified to cause various forms of mild and severe disease conditions, both in man and animal.[1] The SARS-CoV-2 virus originated in 2019 at Wuhan, China from where it spread far and wide resulting in a global pandemic.[2] The virus has phenomenal impact internationally affecting the lives of millions and responsible for the mortality of millions of people. As of 31 October, 2021, according to global updates by the World Health Organization (WHO), nearly 246 million people have been infected with the virus, and 5 million have lost their lives due to CoVID-19 [3] as shown in Figure 01. Initially, information concerning the new virus, SARS-CoV-2 belonging to the coronaviridae family, was considerably scarce, particularly regarding effective treatment of the disease caused by the virus, named as CoVID-19 by WHO. However, as public's health interests created a high demand for information extensive research of SARS-CoV-2 conducted. The virus possesses great similarity with two previously well-known coronaviruses, that are responsible for causing SARS (Severe Acute Respiratory Syndrome) in the year 2002 and MERS (Middle East Respiratory Syndrome) in the year 2012.[4] Thus, the virus was named SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus 2) due to significant resemblances with the SARS-CoV (the virus responsible for SARS).[5]

Spike protein as potential therapetic target

The SARS-CoV-2 virus is an enveloped single-stranded RNA virus, comprising of various non-structural proteins and four main structural proteins: the spike protein (S), envelope protein (E), membrane protein (M) and the nucleocapsid (N).[6] The spike protein (S) is the key protein involved in invasion of virus inside host cells. Envelope protein (E) and the membrane protein (M) play important roles in the viral assembly, while the nucleocapsid protein (N) encloses the genetic material (RNA).[7]

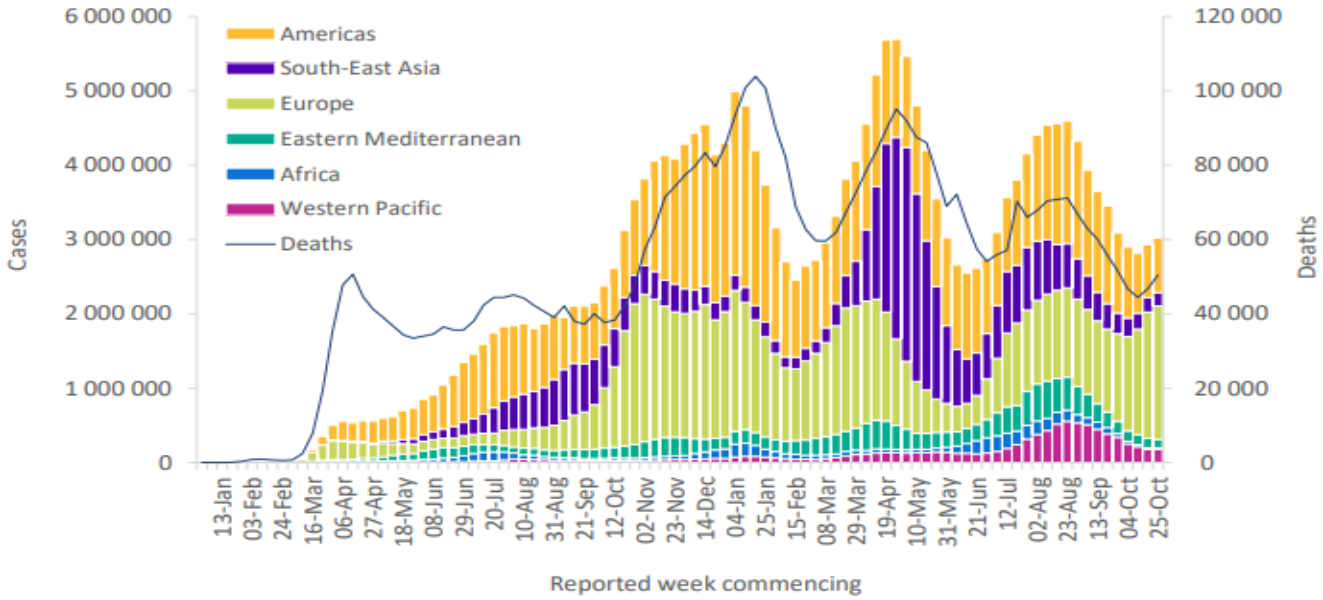

Figure 1: The weekly CoVID-19 reported cases and deaths around the globe October, 2021

The name *corona* (Latin for crown) and the crown-like appearance of coronaviruses occurs due to the presence of the spike proteins which protrude from the viral envelope, all out around the surface of the cell.[8] The spike protein is a surface glycoprotein that attaches to the host cell receptors and promotes viral entry into host cells and triggers the infection process.[9] as shown in Figure 2. Viral entry takes place through two mechanisms via fusion with the host cell membrane or via undergoing endocytosis, in case of which the membranes fuse from within the endosome.[10] Once inside the cell the virus replicates its genetic material, it forms and assemble new virions, which are then released from the cells and infect further cells and proliferate in a similar manner.[11] The spike protein consists of two main functional domains, the S1 domain being responsible for binding with receptors of the cells and the S2 domain that is involved in the fusion of the viral membrane with the host cell membrane.[12] The mode of infection of SARS-CoV-2 occurs along the same mechanism as SARS-CoV, via interaction with ACE2 (Angiotensin converting enzyme 2). ACE2 is a membrane bound peptidase, abundantly present in epithelial cells of the blood vessels, lung, kidney and the intestines, the enzyme is involved in processes of the immune system and the cardiovascular system.[13] Analysis by cryogenic electron microscopy, revealed that though the SARS-CoV and SARS-CoV-2 viruses are similar and both target the ACE2, however the new virus SARS-CoV-2 was found to possess nearly 10-20 times higher affinity for ACE2 than SARS-CoV.[14]

Studies have revealed that viral entry into human cell, and subsequent spread of infection occurs only after the spike protein interacts with ACE2.[15] The essential roles of the spike protein in viral attachment, fusion, entry and infection, have led to it being considered an important and effective potential target in the development of therapeutic agents and vaccines for managing CoVID-19.[16] Infact, the CoVID vaccines currently available, also depend on the viral spike protein for their effectivness.[17] Yet, while various vaccines have been developed, distributed and administered all over the world, the corona pandemic is ongoing, as is the search for new therapeutic agents against the virus. Many previously approved and safe drugs have been investigated, reinvestigated and in some cases being utilized for their activity against the disease, similarly, natural products being a rich source of phytochemicals are also being thoroughly explored in the search of a cure.[18]

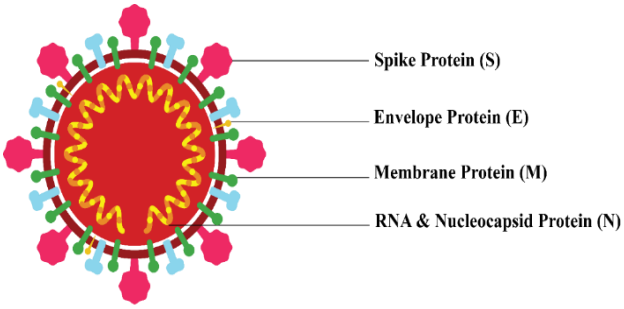

Figure 2: Spike protein as a potential therapeutic target, depicting the main viral structural protein

Methodology

A review of the existing literature was conducted through means of databases including Google scholar, PubMed and ScienceDirect using related keywords such as "SARS-CoV Spike protein", "coronaviruses", "spike protiens", "phytochemicals", "medicinal plants" and "natural products" were used, individually and collectively. Over 76 of the resultant articles were then extensively explored and the relevant information concerned was extracted. Only the data regarding natural plant-derived phytochemicals which could target the Spike protein of SARS-CoV-2 was included. The information about natural products that can target the proteases and those that interfere in replication was excluded. The collected data are discussed and presented in tabloid form to aid in comprehension and understanding.

Discussion

Phytochemicals as candidates to target spike protein

Described in this review, are some phytochemicals that have investigated for their protective roles in the fight against SARS-CoV-2 due to their interactions with the spike protein of the coronavirus. In the initial months of the pandemic, one of the first virtual screening study conducted, analyzed over 40,000 candidates, including FDA approved drugs and natural products obtained from the ZINC database and literature. This study showed that drugs used for the treatment of Hepatitis C (also an enveloped, single stranded RNA virus) could be potentially used for CoVID-19 due to their ability to bind and interfere with the spike protein. The natural compounds that found to be effective were amyrin, loniflavone, procyanidin, phillyrin, proanthocyandin, sericoside, punicalagin, strictinin, rutin and tirucallina.[19]

Traditional Chinese Medicines (TCM) also possess many natural products capable of treating various types of diseases and conditions. The phytochemicals that have shown activity against the spike protein of the human coronaviruses include anthraquinones like emodin and rhein, a synthetic anthraquinone derivative, and a tannin tetra-o-galloyl-d-glucose.[19] Emodin from the genus Rheum and Polygonum exerted its activity by the inhibition of the interaction between the SARS-CoV spike protein and the human ACE2. Tetra-O-galloyl- d-glucose from Galla chinensis and luteolin from Veronicalina riifolia exerted anti-viral by binding with the spike protein of SARS.[20,21] Similarly, a study conducted on thirteen compounds of plants in the TCM system pharmacology (TCMSP) database, discovered a compound Dihydrotanshinone I to possess high binding affinity with the viral spike protein.[22]

Plants belonging to the Glycyrrhiza spp. exert various pharmacological actions and are extensively utilized in the TCM system.[23] Phytochemicals of Glycyrrhiza glabra, particularly the flavonoids (Glycyrrhizin, Glabridin, Liquirtigenin) and constituents including Glycyrrhizic acid and Glycyrrhetinic acid are known to have activity against the SARS-CoV. These agents act through multiple mechanisms, which include influencing the viral attachment between the host cells and spike proteins and by hindering viral replication via effects on the nucleocapsid and functional proteins. The phytochemicals have found to have binding affinity with SARS-CoV-2 through molecular docking studies include glycyrrhetic acid, shinflavanone, glycyrrhizin, glabridin, hispaglabridin a, and glabrin b.[11] An *In-silico* molecular docking study of phytochemicals belonging to Glycyrrhiza glabra comparatively performed against proposed standards (Lopinavir, Rotinavir) for activity against the spike protein, concluded that plant phytochemicals glycyrrhizic acid, liquiritin, glyasperin a and isoliquiritin apioside displayed similar or higher binding activity than the standards. The glycyrrhizic acid showed the highest affinity and is thought to be the most effective spike inhibitors from the constituents of Glycyrrhiza glabra.[24]

Another molecular docking study on 10 naturally occurring compounds against the spike protein of the SARS-CoV-2 revealed three phytochemicals that

presented with the ability to bind and inhibit the interaction between the viral spike protein and the ACE2 receptors. Namely fisetin, quercetin and kaempferol, possess the potential to be explored for *in-vitro* and *in-vivo* studies against the new coronavirus.[25] Curcumin, bisdemethoxycurcumin and demethoxycurcumin, from the curcuma sp., tangeretin, hesperetin, hesperidin, nobiletin, naringenin from the citrus sp., brazilein and brazilin from caesalpinia sappan (sappan wood), galangin and acetoxychavicol acetate from Alpina galangal (Galangal), were found to possess good binding affinity with a binding domain of the spike protein of the SARS-CoV-2 when investigated via molecular docking by researchers in Indonesia. According to this study, the medicinal plants and its phytochemicals could be beneficial in the treatment and prevention of the viral infection, and compounds with high binding affinities could be potential therapeutic agents in the management of CoVID-19.[26]

Hesperidin from valeriana jatamansi, anthraquinones and rhein from Cassia angustifolia, anthraquinones and chyrsin from oroxylum indicum and emodin from rheum emodi have reported as the spike inhibitors for SARS-CoV. Through docking studies, focused on targeting the bound structure of the spike glycoprotein of SARS-CoV-2 and human ACE2, three of the above-mentioned compounds identified as more likely to be beneficial in the treatment of the viral infection. Namely i) hesperidin, a flavonoid present abundantly in lemons and oranges, ii) chyrsin, a flavonoid naturally occurring in honey and propolis, and iii) a polyphenol emodin, present in many plants like aloe vera, senna, rhubarb etc.[27] Acetogenins from Annona muricate, particularly cis-annonacin displayed significant docking properties with high binding affinity and low binding energy and is suggested to be investigated with further studies.[26]

Essential oils are well known for their pharmacological activities, essential oils from different plants aid in the treatment of various acute conditions, chronic diseases and against bacterial and viral infections. A study investigated the anti-viral potential of the constituents of essential oils obtained from plants belonging to the Lamiaceae, Lauraceae, Myrtaceae, Apiaceae, Fabaceae and Geraniaceae families by *in-silico* screening against the spike protein of SARS-CoV-2. This study reported that anethole, cinnamaldehyde, carvacol, geraniol, cinnamyl acetate, thymol, pulegone, L-4-terpineol have the potential to inhibit the spike protein of SARS-CoV-2 and could potentially be effective agents in the treatment of CoVID-19.[27]

In a virtual screening study of 52 plants belonging to the Ayurvedic system medicine, the researchers identified several phytochemicals that displayed promising activities against CoVID-19, which not only had high binding affinity with just the Spike protein (S) of SARS-CoV-2, but also the Papain-like protease (PL-Pro) and the Main protease (M-Pro), that are non-structural proteins necessary for viral replication and lifecycle. The phytochemicals are kuwanon X from Morus alba, punicafolin, emblicanin A, punigluconin, phyllanemblinin A from Phyllanthus emblica, rutin from Azadirachta indica, lithospermic acid from Salvia miltiorrhzia, amarogentin and amaroswerin from Swertia chirata. In this study, the authors suggested that Morus alba and Phyllanthus emblica could prove effective in the treatment of infection with SARS-CoV-2.[25]

In addition, phytochemicals of Mangifera indica, Mukia maderaspatana, Justicia adhota tested for affinity against the SARS-CoV-2 spike protein. Diphyllin and tuberculatin, especially those form the Malabar nut (Justicia adhota) showed significant selective binding affinity with the spike protein, these phytochemicals showed better affinity than even some anti-viral medications and standards.[22]

Kabasura Kudineer is a Siddha formulation (Indian herbal medicine) that is composed of fifteen natural products and has used for the treatment of influenza and fevers accompanied with flu-like- symptoms. JACOM is an Indian herbal formulation that is a combination of five plants, which has shown to be effective against influenza. This medicine when screened *in-silico* against SARS-CoV-2 spike protein in a study, displayed nine phytochemicals that had high affinity with the spike protein. These included magnoflorine from sida acuta, 5-hydroxy-7,8-dimethoxyflavanone from andrographis paniculata, tinosponone from tinospora cardiofolia, cirsimaritin, chrysoeriol and 6-methoxygenkwanin from plectranthus amboinicus, quercetin and vasicinone from justicia adhatoda, and lastly luteolin from Costus speciosus. In the fore mentioned study, the authors concluded with an intent to utilize these six plants, containing phytochemicals with anti-viral activity and develop an effective novel herbal formulation (SNACK-V) against SARS-CoV-2.8 Table 1).

Table 1: Potential phytochemicals with their plant sources reported to target the spike protein.

Sr.	Phytochemical	Class	Plant source	Reference
1.	5-Hydroxy-7,8-dimethoxyflavanone	Flavonoid	*Andrographis paniculata*	8
2.	Amarogentin	Glycoside	*Swertia chirata*	17
3.	Amaroswerin	Glycoside	*Swertia chirata*	17
4.	Anethole	Volatile oils	Apiaceae, Fabaceae, Geraniaceae Lamiaceae Lauraceae Myrtaceae	9
5.	Carvacol			
6.	Cinnamaldehyde			
7.	Cinnamyl acetate			
8.	Geraniol			
9.	Thymol			
10.	Pulegone			
11.	L-4-terpineol			
12.	Brazilein	Aromatic hydrocarbon	*Caesalpinia sappan*	23
13.	Brazilin	Heterocyclic compound	*Caesalpinia sappan*	23
14.	Chyrsin	Flavonoid	*Oroxylum indicum*	1
15.	Cirsimaritin	Flavonoid	*Plectranthus amboinicus*	8
16.	Chrysoeriol	Flavonoid	*Plectranthus amboinicus*	8
17.	6-Methoxygenkwanin	Flavonoid	*Plectranthus amboinicus*	8
18.	*cis*-Annonacin	Acetogenins	*Annona muricate*	16
19.	Curcumin	Curcuminoids	*Curcuma sp.*	23
20.	Demethoxycurcumin	Curcuminoids	*Curcuma sp.*	23
21.	Bisdemethoxycurcumin	Curcuminoids	*Curcuma sp.*	23
22.	Diphyllin	Lignan	*Justicia adhota*	17
23.	Tuberculatin	Diphyllin glycoside	*Justicia adhota*	17
24.	Emodin	Anthraquinones	*Rheum emodi* *Rheum* and *Polygonum* (Genus)	1, 26
25.	Fisetin	Flavonoid	Fabaceae	15
26.	Galangin	Flavonoid	*Alpina galangal*	23
27.	Acetoxychavicol acetate	Phenol ester	*Alpina galangal*	23
28.	Glabridin	Flavonoid	*Glycyrrhiza sp.*	11, 21
29.	Glyasperin A	Flavonoid		
30.	Glycyrrhetic acid	Triterpenoid		
31.	Glycyrrhizin	Triterpenoid		
32.	Glabrin B	Flavonoid		
33.	Liquiritin	Flavonoid		
34.	Hispaglabridin A	Flavonoid		
35.	Isoliquiritin apioside	Flavonoid		
36.	Shinflavanone	Flavonoid		
37.	Hesperetin	Flavonoid	*Citrus sp.*	23
38.	Nobiletin			
39.	Naringenin			
40.	Tangeretin			
41.	Hesperidin	Flavonoid	*Citrus sp Citrus aurantium* *Valeriana jatamansi*	1, 23
42.	Kamferol	Flavonoid	Angiospermae	15
43.	Kuwanon X	Flavonoid	*Morus alba*	17
44.	Lithospermic acid	Flavonoid	*Salvia miltiorrhzia*	17
45.	Luteolin	Flavonoid	*Costus speciosus* *Veronicalina riifolia*	8, 26
46.	Magnoflorine	Alkaloid	*Sida acuta*	8
47.	Punicafolin	Tannin	*Phyllanthus emblica*	17
48.	Emblicanin A	Flavonoid glycoside	*Phyllanthus emblica*	17
49.	Punigluconin	Tannin	*Phyllanthus emblica*	17
50.	Phyllanemblinin A			
51.	Phillyrin	Lignan	*Forsythia suspensa*	7
52.	Proanthocyandin	Flavonoid	*Vitis vinifera*	7
53.	Punicalagin	Tannin	*Terminalia catappa*	7

54.	Quercetin	Flavonoid	*Justicia adhatoda*	8, 15
55.	Vasicinone	Alkaloid	*Justicia adhatoda*	15
56.	Rhein	Anthraquinones	*Cassia angustifolia*	1
57.	Rutin	Flavonoid	*Azadirachta indica*	17
58.	Sericoside	Triterpenoid	*Terminalia sericea*	7
59.	Strictinin	Tannin	*Camellia sinensis*	7
60.	Tetra-O-galloyl-d-glucose	Anthraquinones	*Galla chinensis*	26
61.	Tinosponone	Active constituent	*Tinospora cardiofolia*	8
62.	Tirucallin A	Tannin	*Euphorbia tirucalli*	7
63.	Dihydrotanshinone	Quinone	*Salvia miltiorrhiza*	22

Conclusion

This new coronavirus continue to threaten, infect and take the lives of people all over the world. The interaction between human/host cell ACE2 receptors and the viral spike protein has led to an increased interest in agents that can inhibit the actions of the spike protein and subsequently viral infection and entry into the cells. In this review, phytochemicals that have found to possess anti-viral activities due to their binding affinities and binding energy values via *in-silico* molecular docking studies against the coronavirus spike protein have compiled. Data of more than 60 phytochemicals belonging to various classes, including alkaloids, anthraquinones, flavonoids, glycosides, lignans, quinones, saponins, tannins, triterpenoids and volatie oils were summarized in this review. These plant-derived phytochemicals can be explored (*in-vitro*, *in-vivo*) and developed further as therapeutic agents against the SARS-CoV-2 virus.

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CASE REPORT

Niemann-pick disease: Type A presenting as a case of protein energy malnutrition

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Author`s Contribution

[1] Manuscript presentation, follow up of patient
[2] Communication with patient, Data Collection
[3] literature Review, data review

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A B S T R A C T

We hereby report a rare case of a young child with Niemann-Pick disease who had multiple hospital admissions due to repeated gastrointestinal and respiratory tract infections. The disease is overall quite rare in our population however, our case highlights the fact that in any young child with repeated infections of unknown etiology, this condition should be considered and evaluated.

Keywords: *Niemann-pick, protein-energy malnutrition*

Introduction

Niemann-pick is a rare genetic disease. It is autosomal recessive in inheritance with deficiency of a lysosomal enzyme called acid sphingomyelinase.[1] This results in lysosomal accumulation of sphingomyelin into various body organs. It is classified into four classical variants or types. Type A presents at an early age occurs because of missense mutation causing absolute deficiency of sphingomyelinase and can be life threatening in early period of infancy. Symptoms include feeding difficulties, failure to thrive and recurrent respiratory tract infections due to reduced lung capacities. Affected children have hypotonia and diminished tendon reflexes.[1] In type B, there is hepatic impairment, low platelets count, lungs involvement and visual changes. Common symptoms include recurrent respiratory tract infections, jaundice and some children may develop cirrhosis.

Type C Niemann-pick disease is characterized by visceral involvement including enlargement of liver, splenomegaly, neurological impairment, abnormal eye movements and psychiatric manifestations.[2] Neurological involvement is more likely in Type C as compared to Type B.[3] Type D is currently recognized as variant of Type C and occurs due to accumulation of cholesterol and sphingomyelin. It's more common in Nova Scotia hence also termed as "Nova Scotia" variant. Treatment of Niemann pick disease involves multidisciplinary approach including treatment of complications and rehabilitation, till now no treatment has proven to be curative.[4]

Case report

A one and half years old male, diagnosed case of Niemann-pick disease type A presented to the OPD of tertiary care hospital in Islamabad with presenting complaints of vomiting and diarrhea for 1 day as shown in Figure 1. There were 2 episodes of vomiting with a small quantity of yellow vomitus, and contained milk with food particles. No fever and no abdominal pain was recorded. Diarrhea was characterized as watery, loose with a frequency of 8 to 10 episodes per day. There was no mucous or blood in stool. Past history revealed repeated hospital admissions due to respiratory tract infections and gastroenteritis.

The developmental milestones were delayed including delay in raising the head while in lying position, poor response while calling his name at age of one year, inability to get up from lying position without support. He was diagnosed as Niemann pick disease type A through genetic testing with a positive homozygous pathological variant identified in SMPD 1 gene in a blood sample. The genetic testing revealed that the concentration of the lyso-SM-509 biomarker was pathologically increased and activity of acidic sphingomyelinase was pathologically decreased.[5]

On General physical examination, patient was afebrile and lethargic. Blood pressure was 90/50 mmHg and pulse rate was 128/minute. He was dehydrated with presence of pedal edema. On examination of the abdomen, there was generalized abdominal distension. The spleen was palpable crossing the umbilicus. Bowel sounds were audible. The patient was then admitted to the hospital for further management and discharged after stabilization and correction of dehydration.

Figure 1: A one and half years old male, diagnosed case of Niemann-pick disease with the following investigation mentioned in Table 1.

Table 1: Investigation of patient

Investigations	Results
Hb	7.1
TLC	7900
Platelets	66000
CRP	16
Serum Albumin	<2.5
Serum Electrolytes: Na K Cl HCO3 BUN	 138 2.5 107 21 6
Cr	0.2
LFTs: ALT AST ALP	 367 60 105
Apt	49 Sec
PT	17.2

Discussion

The patient presented in our case report had multiple indoor admissions with repeated respiratory tract and gastrointestinal infections. His presenting clinical features especially splenomegaly, thrombocytopenia, anemia; delayed developmental milestones were suggestive of malnutrition disorder.

Although these clinical features typically resemble to those seen in already reported cases of Niemann pick disease and we didn't see any unusual/atypical feature in our case, however the purpose of discussing this case is to highlight the importance of evaluation of storage disorders in our population. In every child who presents with repeated infections, organomegaly and delayed milestones, we should consider evaluation of storage disorders.

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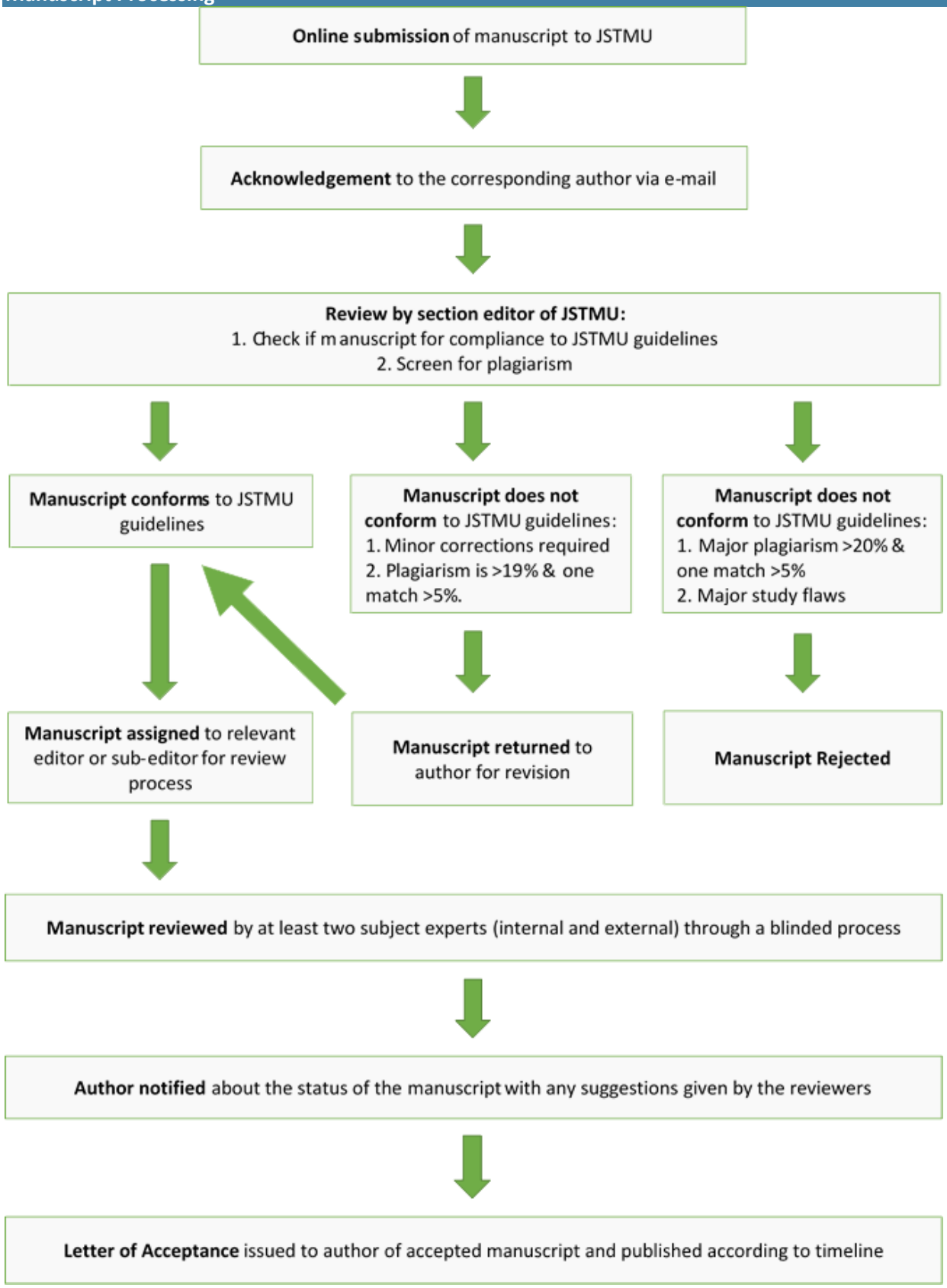

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PG Thesis / Dissertation based articles

An article based on dissertation can be sent for publication provided that the data is not more than three years old. A copy of approval letters of synopsis and dissertation obtained from the review board must be submitted with the research paper. Dissertation based articles should be re-written in accordance with the journal's instructions to the author guidelines.

Article shall undergo routine editorial processing including external peer-review based upon which final decision shall be made for publication. Such articles, if approved, shall be published under the disclosure by author that 'it is a Dissertation based article'.

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On publication, the corresponding author will be sent the URL for online access to their article along with a hard copy to his postal address through courier. Reprint requests are entertained by the editor on additional reprint charges as per prevailing rate on cost-to-cost basis.

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INSTRUCTIONS FOR AUTHORS

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.

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

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

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

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.

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

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