Volume: 6, Issue: 1
Jul - Dec 2023

ISSN (Print): 2312-6531
ISSN (Online): 2958-5511

Foundation University Medical Journal

Foundation University Islamabad,
Defence Avenue, DHA Phase-I,
Islamabad 44000, Pakistan.
https://fumj.fui.edu.pk
fumj@fui.edu.pk

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Foundation University Medical Journal

Vol. 6, No. 1, Jul - Dec 2023
ISSN Print: 2312-6531
ISSN Online: 2958-5511

For electronic submission of articles (OJS)/ Online Issue:
fumj.fui.edu.pk

Email address for correspondence:
fumj@fui.edu.pk

Publication Office: Department of Pharmacology, Foundation University Medical College, DHA Phase - I, Islamabad, Pakistan 46000

FOUNDATION UNIVERSITY MEDICAL JOURNAL

Vol-6, No.1, Jul - Dec 2023

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EDITORIAL

ESCAPE ROOMS IN MEDICAL EDUCATION AND TRAINING

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Simulation-based education is gaining increasing recognition as an effective teaching method in medical education; placing learners at the center of innovative and learner-centered models.[1]

One of such methods is Escape rooms, which have emerged as a valuable simulation-based tool in medical education, offering a unique approach to learning.[2] Healthcare simulation escape rooms engage students in an interactive way incorporating clues and puzzles to solve tasks related to healthcare themes.

Incorporating game elements into non-game contexts (gamification) is an immersive experience grounded in educational theory. It caters to the needs of modern learners like millennial students which makes it popular.

Escape rooms motivate learners, increase engagement, and encourage social interaction, making them an ideal fit for medical education. They align with Kolb's experiential learning theory, offering concrete experiences that promote reflective observation and active experimentation.[3] They provide opportunities for team building, skills development, knowledge acquisition, and educational research.

The medical training benefits of escape rooms can be explored by case studies and theoretical perspectives.

Team Building: A study involving core medical trainees demonstrated that escape rooms can enhance teamwork, communication, and awareness of individual strengths and weaknesses.[4] The escape room experience allowed participants to learn about peer capabilities and adaptability in time-pressured situations.

Research Tool: In another study, an escape room was used as an adjunct to traditional dermatology lectures for clinical-stage medical students. It served both as a method to present dermatological content and as a research tool to assess student perceptions of dermatology as a specialty.[5] This showcases the versatility of escape rooms in fulfilling multiple academic and educational purposes.

Learning Tool: Escape rooms have also been useful in high-pressure clinical specialties like obstetrics. Trainees were challenged with solving clues related to clinical processes, promoting effective teamwork and communication. Participants reported that they acquired valuable skills applicable to real-life clinical practice.

The popularity of escape rooms in education can also be attributed to several factors:

Millennial Learners: Millennials, who dominate the current medical education cohort, are technologically adept and value collaborative learning thus aligning escape rooms with these preferences for interaction.

Gamification: The incorporation of game elements into non-game contexts, reverberates with millennials.[6] Escape rooms are thus ideal for motivating learners and increasing and encouraging social engagement.

Convenience: Escape rooms offer discrete, time-efficient learning experiences that can be completed in less than an hour. They are cost-effective and do not require expert facilitators, making them a convenient choice for medical curriculum delivery.

The following analysis shows how Escape Rooms are strongly aligned with educational theory in several ways:

Experiential Learning: Escape rooms effectively follow Kolb's experiential learning cycle, enabling active experimentation in a safe environment and emphasizing the importance of debriefing and reflection.

Gamification and Motivation: Self-determination theory highlights the role of autonomy, competence, and relatedness in motivation. Escape rooms set achievable goals, offer freedom of choice, and promote effective teamwork, enhancing participants' motivation to learn.[7]

In conclusion, escape rooms have emerged as a powerful educational tool in the field of medical training, aligning with the needs and capitalizing on the preferences of today's learners, particularly millennial medical students. The theoretical perspectives show that escape rooms offer a multifaceted approach to learning, enhancing various aspects of medical education. Grounded in educational theory, they offer a flexible and effective means of teaching a range of skills and knowledge while promoting student teamwork and engagement.

Escape rooms offer a means of delivering quality education in a timely and cost-effective manner, without compromising patient contact or clinical time. Furthermore, their alignment with established educational theories, such as Kolb's experiential learning, reinforces their value as a pedagogical tool.

In essence, escape rooms have transcended their origins as entertainment and evolved into an integral component of modern medical education. They are a compelling choice for educators and institutions seeking innovative ways to prepare the healthcare professionals of tomorrow. As the landscape of medical education evolves, escape rooms are poised to play an increasingly significant role in shaping the future of healthcare training.

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RESEARCH ARTICLE

EXAMINATION OF PERCEIVED BARRIERS RELATED TO EXERCISE AMONG UNDERGRADUATE FEMALES

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ABSTRACT

Introduction: *Physical activity is crucial for the well-being of young females, especially undergraduates, in the prevention and management of non-communicable illnesses.*

Objective: *To determine perceived exercise barriers among undergraduate females and their associations with sub-scales.*

Design: *A cross-sectional survey*

Place and duration: *University of Lahore and the University of Gujrat from April 27 to August 25, 2023*

Methods: *A cross-sectional survey was conducted on 361 female undergraduates at the University of Lahore and the University of Gujrat using the Exercise Benefits and Barriers Scale (EBBS). Population proportion was estimated at 95% confidence interval.*

Results: *The study revealed that a majority of participants (63.4%) fell within the age range of 20-25 years, while 36.3% were below 20 years old. Various obstacles were identified, such as challenges related to the exercise environment, time availability, physical exertion, and lack of family support. Notably, factors like embarrassment, time constraints, physical effort, and family discouragement exhibited significant correlations with specific aspects of the study, all with a highly significant level of <0.05. On the other hand, perceived advantages demonstrated a robust and notably strong significance in the findings.*

Conclusion: *Perceived exercise barriers are consistent among undergraduate females, with embarrassment, time constraints, physical exertion, and family discouragement being the key obstacles. Understanding these sub-scale associations can guide targeted interventions to promote physical activity. Tailored interventions addressing specific sub-scales can effectively address exercise barriers, enhancing physical activity among undergraduate females.*

Keywords: *Exercise Adherence, Exercise Participation, Perceived Barriers, Sedentary Lifestyle, Undergraduate Females.*

INTRODUCTION

Physical activity (PA) is a crucial component of overall well-being, encompassing a wide range of movements, from daily tasks to leisure activities. The absence of PA during youth can significantly increase the risk of non-communicable diseases, such as cardiovascular disease, cancer, and osteoporosis, while also promoting sedentary lifestyles and obesity.[1] Modernization and daily life stressors have transformed the traditional human lifestyle. Regular engagement in PA is vital for maintaining good health and preventing musculoskeletal issues and various chronic conditions. Adolescence marks a critical period for establishing lifelong PA habits.[2] Despite the well-documented health benefits of PA, specific barriers to exercise among young females remain understudied.[3]

Several factors, including societal norms and personal demands, can obstruct regular PA engagement, particularly in leisure time.[4] These obstacles are both internal and external, encompassing individual attitudes and environmental factors.[5] Understanding the complexities of inadequate PA participation involves personal, interpersonal, environmental, and policy-

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Received: 13 Oct 2023; revision received: 19 Dec 2023; accepted: 21 Dec 2023

related influences. Enhancing this understanding is vital to develop effective strategies for women's health promotion through increased PA.[6] Regular PA has extensive health benefits, including reducing the risk of heart disease, hypertension, diabetes, and obesity, in addition to improving mental well-being. Unfortunately, many individuals fail to incorporate sufficient PA into their routines. [7]

Recent trends reveal a decline in PA levels among female college students, posing health risks.[8] Women are generally less active than men, impacting their risk of obesity.[9] Non-communicable diseases pose a significant health threat in Pakistan, particularly for women due to higher rates of inactivity and obesity.[10] Motivation to engage in PA is influenced by demographic, psychological, behavioral, social, and environmental factors.[11] Gender disparities exist in leisure-time PA.[12]

The presented research aimed to examine perceived barriers to exercise among undergraduate females, shedding light on the factors that hinder their engagement in regular physical activity.

METHODS

The research employed a cross-sectional, quantitative approach conducted at the University of Gujrat and the University of Lahore, and targeted female undergraduate students. Data collection took place from April 27 to August 25, 2023, encompassing a sample size of 361 participants. A convenient non-probability sampling method was utilized for participant selection. Sample (n = 361) was calculated at 95% confidence interval with specified absolute precision 0.05. Inclusion criteria encompassed female undergraduate students aged between 18 and 30 years. Exclusion criteria were defined to exclude individuals with physical impairments or injuries that could impede their participation in physical activity, such as amputations, spinal cord injuries, fibromyalgia, chronic back pain, or chronic obstructive pulmonary disease (COPD). Additionally, individuals who declined to participate in the survey were also excluded from the study.

The primary data collection instrument employed for this study was the exercise benefits and barriers scale (EBBS). The EBBS provides valuable insights into the exercise-related factors that influence this specific demographic, shedding light on the barriers that may deter young female students from engaging in physical activity. Prior to data collection, all necessary ethical approvals from the faculty of allied health sciences research ethics committee was obtained, ensuring that research adhered to ethical guidelines. Considering the sensitivity to cultural differences, the norms and values of the participants was ensured.

RESULT

TABLE I: Characteristics of the participants (n = 361).

	Age	Weight	Height
Categories	N	%	%
Less than 20	131	36.3%	36.3%
20 to 25	229	63.4%	63.4%
Above 25	1	0.3%	0.3%
total	361	100%	100%

The majority of respondents (63.4%) were between the ages of 20 and 25. Only a very small percentage (0.3%) was above the age of 25.

A low *p* value in table II (typically less than 0.05) is indicating that the relationships observed are unlikely to have occurred by chance. The results underscore the diverse reasons why individuals might perceive obstacles to engaging in regular exercise, ranging from practical and logistical concerns to social and psychological factors.

DISCUSSION

Numerous studies have investigated perceived advantages, disadvantages, and factors related to exercise among diverse populations. In 2022, Shava et al. conducted a cross-sectional study on undergraduate students in Zimbabwe, result indicated food insecurity and (CMDS) risk were associated with barriers to exercise.[13] In 2021, an investigation on perceived advantages and disadvantages of exercise among active and inactive university students revealed that the inactive group experienced more exercise barriers, especially related to the exercise environment and physical exertion.[14] O'Dwyer et al. explored the perspectives of adults with ankylosing spondylitis on physical activity and exercise, identifying benefits and barriers to physical activity, including resource limitations, negative attitudes, misinformation, and condition-related challenges.[15]

A study by Jeffery Anak Stephen et al. in 2019-2020 assessed undergraduates at Unimas engaged in physical activity, finding that 74.1% were active, with predictors such as perceived benefits, perceived barriers, and self-rated ability significantly correlating with physical activity levels.[16] Ratnakumar et al. conducted a cross-

Table II: Degrees of freedom and significance of each question on the exercise barrier scales.

Perceived barriers items	Chi-Square	df	Asymp. Sig.
Exercise environment sub-scale			
9: Places for me to exercise are too far away	127.654	3	0.000
12:I am too embarrassed to exercise	118.657	3	0.000
14: It costs too much money to exercise	112.584	3	0.000
16: Exercise facilities do not have convenient schedules for me	137.316	3	0.000
28: I think people in exercise clothes look funny	65.227	3	0.000
42: There are too few places for me to exercise	171.776	3	0.000
Time expenditure sub scale			
4: Exercising takes too much of my time	110.745	3	0.000
24: Exercise takes too much time from family relationships	146.934	3	0.000
37: Exercise takes too much time from my family responsibilities	99.044	3	0.000
Physical exertion sub-scale			
6: Exercise tires me	164.817	3	0.000
19:I am fatigued by exercise	127.875	3	0.000
40: Exercise is hard work for me	134.533	3	0.000
Family discouragement subscale			
21: My spouse (or significant other) does not encourage exercising	94.213	3	0.000
33: My family members do not encourage me to exercise	66.579	3	0.000

sectional study in 2022 on post-stroke depression patients, highlighting significant differences in perceived exercise barriers and enablers between active and non-active groups, with exercise-related fatigue being a major barrier.[17]

The study's findings were organized into two tables, showcasing participant characteristics, perceived exercise barriers, and the relationship between perceived exercise benefits and sub-scales. This discussion delves into the implications of these results in light of previous studies and underscore their significance.

Comparative Analysis

The demographic distribution of participants in this study revealed a noteworthy majority (63.4%) within the age range of 20 to 25 years, aligning with previous research by Smith et al. (2019) that emphasized the pivotal role of college-age women in understanding exercise behaviors.[13] This alignment indicates consistent challenges and barriers related to exercise among this demographic, reinforcing the significance of targeted interventions. Notably, a substantial proportion (36.3%) of respondents were below 20 years old, signifying early concerns about exercise engagement among young females. Additionally, the limited representation (0.3%) of participants above 25 years old indicates the study's focus on the undergraduate population.

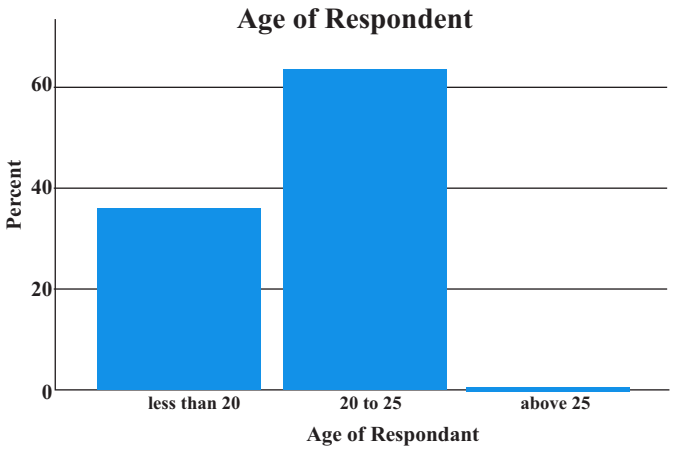

Figure 1: Age distribution of respondents.

Insights from Barriers to Exercise

Table II provided crucial insights into perceived barriers to exercise, showcasing significant associations consistent with prior studies. Factors like embarrassment, body image concerns, cost-related barriers, and inconvenient schedules, lack of exercise spaces, time constraints, physical exertion concerns, and family discouragement displayed associations in line with existing research findings.

Aligning Findings with Prior Research

The alignment of our study's findings with prior research underscores the persistent impact of sociocultural influences on exercise avoidance among women. Sociocultural factors such as media portrayals of idealized body images and financial constraints emerge as consistent barriers. Understanding these influences becomes pivotal for tailoring effective interventions to address specific barriers.[18,19]

Implications and Comparative Analysis

This research closely parallels previous studies, providing deeper insights into sub-scale associations and how barriers manifest across various facets among undergraduate females. The systematic analysis of these associations enhances our comprehension of exercise barriers during this pivotal life stage, aiding in the development of targeted interventions.[16,17,20]

Implications for Intervention

Understanding perceived exercise barriers is crucial for designing effective interventions. This study emphasizes the necessity for multifaceted strategies considering accessibility, affordability, time management, and emotional factors. Tailored programs addressing cultural sensitivities, family influences, and collaborations with educational institutions could systematically address these barriers and promote physical activity among undergraduate females.

CONCLUSION

Perceived exercise barriers are consistent among undergraduate females, with embarrassment, time constraints, physical exertion, and family discouragement being the key obstacles. Understanding these sub-scale associations can guide targeted interventions to promote physical activity. Tailored interventions addressing specific sub-scales can effectively address exercise barriers, enhancing physical activity among undergraduate females.

LIMITATIONS

The associations found must be investigated by other types of studies due to the cross sectional nature of the current investigation the result cannot be applied to larger population, in order to more effectively understand the causation of the topic under study.

RECOMMENDATIONS

To address exercise barriers among undergraduate females, continuous research is essential to adapt intervention strategies. Universities can offer tailored on-campus exercise programs, raise awareness about the benefits of physical activity, and create feedback channels for student input. Periodic program evaluations ensure their effectiveness.

FUNDING INFORMATION

This work received no specific grant from any funding agency in the public, commercial or not for profit sectors.

Author's Contributions:
Following author has made substantial contributions to the manuscript as under:

Sumaira Bibi: Conception of study / Designing / Planning, Manuscript Writing, Experimentation / Study Conduction, Critical Review, Analysis / Interpretation / Discussion, Facilitated for Reagents / Material Analysis.

ACKNOWLEDGEMENT

Dr. Faiza Asghar, The University of Lahore, contributed to the critical review of the article, provided intellectual input, and approved the final version.

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RESEARCH ARTICLE

COVID-19 VACCINE HESITANCY AND ITS RELATED FACTORS AMONG GENERAL POPULATION OF ISLAMABAD, PAKISTAN

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ABSTRACT

Objective: *To determine the proportion of individuals hesitant to COVID-19 vaccination amongst general population in Pakistan.*

Design: *Descriptive Cross-sectional study.*

Place and duration: *Islamabad from September 2021 to September 2022*

Materials and Methods: *The study was conducted on 97 participants recruited by convenient sampling. Data were collected from market and malls of Islamabad while excluding health care professionals and auxiliaries through interviews using self-developed questionnaires.*

Results: *The data were compiled by using SPSS Version 23.0. The study revealed certain peculiar trends, where out of 97 respondents, individuals aged more than 28 years in undergraduate or postgraduate education programs proved more hesitant to vaccination. Most common reason was fear of side effects (61.7%). However, a decrease in hesitancy rate from initial hesitant 54.6% to still hesitant 22.68% was observed among certain individuals. Most and least common vaccines received were Sinovac 33% and AstraZeneca 2.1% respectively.*

Conclusion: *It is inferred that there is a decline in hesitancy towards COVID-19 vaccination from initial days till date. But still remarkable number of participants are reluctant to get vaccination mostly due to fear of its side effects. With awareness program and focused strategy this can be further reduced; leading to eradication of misconceptions and enhanced vaccine compliance.*

Keywords: *COVID-19, Vaccine Hesitancy, General population*

INTRODUCTION

The first human case of COVID-19 was caused by the novel coronavirus, subsequently named SARS-CoV-2 which was first reported by officials in Wuhan City, China, in December 2019 and was declared a pandemic on 11 March 2020 by WHO.[1,2] The pandemic has left a global impact socioeconomically and by landing a severe burden on the healthcare system.[3] It has also rendered a negative psychological impact on the people and strategies should be sought to control it.[4]

Different factors have played role in vaccine hesitancy like poor education, lesser income, safety, confusing messages, mistrust in the medical industry, low confidence in the COVID-19 vaccine and the health service response during the pandemic, worse perception of government measures, perception of the information provided as inconsistent and contradictory.[5]

Moreover, these hesitancy rates can be attributed to different conspiracy theories like fear of it being more harmful than safer, a cause of infertility, chips being inserted, social media platforms as the main source of misinformation. Respondents who depended on medical doctors, scientists and scientific journals were the least likely to harbor conspiracy beliefs.[6]

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Received: 12 Jul 2023; revision received: 19 Dec 2023; accepted: 21 Dec 2023

Other pulling factors included respondents reporting higher levels of trust in information from government sources and employer requirement. [7] A more acceptance rate was also present in health care workers. [8]

A study done in Cameroon showed vaccine hesitancy of 84.6% [9] while it is 56%, 35% and 31% in Portugal, Ireland and UK respectively.[10, 11] Study conducted in Australia showed 29% with low levels of hesitancy and 7% had high level of hesitancy. [12]

Despite the availability of safe and effective vaccines, the refusal to get vaccination leads to recurrent outbreaks of vaccine-preventable diseases. In order to achieve the common goals of eradicating certain infectious diseases and to protect individual health, it is pertinent to understand the fundamentals of vaccine hesitancy. The 5C model describes five relevant psychological antecedents of vaccination: confidence, risk perceptions, constraints, calculation (extent of information search), and collective responsibility (willingness to protect the community). Structural changes to reduce practical barriers are important to improve vaccine compliance. [5]

The present study were conducted to observe hesitancy proportions, key misconceptions regarding vaccination against COVID-19 in Pakistan and the factors responsible for the inclination towards vaccination. It will help the authorities of a country with scanty resources, like Pakistan, in developing and adopting a focused strategy to eliminate the misconception, thereby enhancing the vaccination compliance markedly

METHODOLOGY

This descriptive cross-sectional study was done on a sample size of 97 which was calculated by WHO sample size software keeping confidence interval 95%, absolute precision 0.1 and 50% prevalence to get maximum appropriate response. Approval from IRB Fazaia Medical College was taken before initiation of study. Data were collected after approval from the adult population of Islamabad who were present in public places like central markets or malls. Health care workers like doctors, nursing staff, doctors of physiotherapy, doctors of pharmacy and medical students were excluded from this study. Duration of study was one year from September 2021 - September 2022. A self-developed questionnaire was used to collect the relevant information. Validity of questionnaire was assessed by applying content validity ratio. The questionnaire comprised of permission from individuals, socio-demographic characteristics and questions pertinent to vaccine hesitancy. Participants were recruited using non-probability convenient sampling and after taking informed consent, the participants were interviewed by pre-trained researcher themselves in National language of Pakistan that is Urdu. They were briefed about their right to withdraw whenever they like and regarding confidentiality and anonymity of their personal information. Data compilation and analysis was done by using the SPSS version 23.0. Percentages mean and standard deviation were computed for certain variables in descriptive statistics. Cross tabulation was done and chi square test was applied to assess its statistical significance.

RESULTS

Out of 97 respondents, 53.6% (n=52) were males with a majority age group being less than or equal to 27 years (n=72). A large number of participants 69% (n=67) were educated till graduation or post-graduation.

Further data analysis revealed that 89.7 % (n=87) were vaccinated and rest were not. Among those who were vaccinated, only 15.5% (n=15) were fully vaccinated with booster dose, while 78.1% (n=68) received 2 doses of vaccines and only 4.5% (n=4) received single dose. Out of all those who received booster, the most common reason was to work abroad 6.2 % (n=6) and to boost immunity 6.2 % (n=6).

Respondents who got sick by COVID-19, 10.3% (n=10) got covid before getting vaccination and 9.3% got COVID after being completely vaccinated (n=9). After receiving 1st dose of vaccination, 6.2% (n=6) of the population got COVID. A single case was seen where the person contracted covid before getting vaccination and also had covid after getting fully vaccinated (n=1). A majority of 73.1 % of respondents (n=71) never got sick by COVID.

Most common vaccine received was Sinovac 33 % (n=32) followed by Sinopharm 19.6 % (n=19). Least common vaccination received was from AstraZeneca 2.1 % (n=2).

In this study, individuals who were hesitant to get vaccination when the vaccine was first introduced were labeled as initial hesitant and those who didn't change their mind and were hesitant up till date were labeled as

still hesitant

Out of 97 respondents, 54.6 % (n=53) were initially hesitant. Further question revealed that 22.68 % (n=22) of the 92 respondents were still hesitant. However, majority of them (72.16%) were not found to be still hesitant (n=70) (Figure 1).

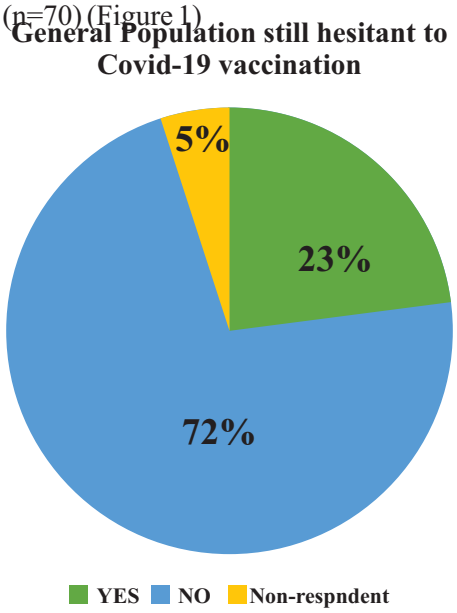

Figure 1: General population still hesitant to COVID-19 vaccination

Table I shows the pulling factors of COVID-19 vaccination as depicted by study participants, who were allowed to pick more than one pulling factor in a close ended question having multiple options. Out of the 88 who responded to this question, only one was unvaccinated.

Most common pulling factor for receiving vaccine was to protect the loved ones from contracting the virus (35.2 %) followed by pre-requisites to get back to work (30.68 %) and encouragement by a friend or a family member (26.1 %).

Table II shows proportion of participants who were given multiple options and were allowed to pick more than one pushing factor to receive vaccination.

Most common pushing factor to receive vaccination was that people (61.7%) were scared of the side effects (n=29) and 29.7 % of the people were worried that vaccine is not properly tested and made in a short span of time (n=14).

Table I: Pulling factors to receive covid-19 vaccination

Pulling Factors	Frequency (n) 88	Percentages (%)
Protection of loved ones from contracting the virus	31	35.2%
Pre-requisite to get back to work.	27	30.68%
Encouraged by a friend or a family member.	23	26.1%
Media awareness that cleared misconceptions	19	21.59%
Others	12	13.6%
Free availability	11	12.5%
Media encouragement to get covid - 19 vaccination	11	12.5%
If I catch a virus, vaccination will reduce its severity	07	7.95%
Someone I know died of corona	07	7.9%
I have to travel abroad	03	3.40%

Table II: Pushing factors for COVID-19 vaccination in those who are still hesitant to receive

Pushing factors in those who are still hesitant	Frequency (n) 47	Percentages %
Scared of side effects	29	61.70%
Worried that vaccine is not properly tested and made hurriedly	14	29.7%
Vaccine might be ineffective to prevent me from contracting the virus.	07	14.89%
It can cause infertility.	06	12.76%
Impact of corona is highly exaggerated	6	12.76%
Vaccine made in Europe and America is safer than Chinese vaccine available in our region	04	8.5%
Receiver of vaccine dies within 2 years	03	6.38%
Corona virus does not exist	03	6.3%
In disguise of corona vaccination nano chips are being inserted	03	6.38%
I have a health condition so cannot receive vaccination	02	4.25%
Other	02	4.25%

Cross tabulation (Table III) of socio-demographic characteristics with initial hesitancy towards vaccination showed significantly high hesitancy among females (68.9%) than males (42.3 %) (p=0.014).

Population aged ≥ 28 years were more hesitant towards vaccination (72 % n=35) as compared to people of age ≤ 27 (48.6 % n=18). However, chi square showed no statistically significant difference in this regard. Similarly, people doing graduation and masters had high hesitancy rate but remained statistically insignificant.

Table III: Cross-tabulation of socio-demographic characteristics with initial hesitancy towards covid-19 vaccination

	Initial hesitancy			*p*-value
Gender	**Yes N (%)**	**No N (%)**	**Total N (%)**	
Female	31(68.9%)	14(31.1%)	45(100%)	0.014*
Male	22(42.3%)	30(57.7%)	52(100%)	
Age	**Yes**	**No**	**Total**	
≤27 yrs	35(48.6%)	37(51.4%)	72(100%)	0.062
≥28 yrs	18(72%)	07(28%)	25(100%)	
Education	**Yes**	**No**	**Total**	
Matric	04(50%)	04(50%)	8(100%)	0.563
F. A	04(50%)	04(50%)	8(100%)	
FSC	06(42.9%)	08(57.1%)	14(100%)	
B. A	11(47.8%)	12(52.2%)	23(100%)	
BSC/BBA	10(62.5%)	06(37.5%)	16(100%)	
MSC/MA	14(73.7%)	05(26.3%)	19(100%)	
ENGINEERING	04(50%)	04(50%)	8(100%)	
MBA	0(%)	01(100%)	1(100%)	

DISCUSSION

COVID-19 pandemic had put a lot of strain on health services globally, initially the lack of vaccine led towards practicing of non-pharmacological measures like social distancing, wearing of mask and hand hygiene.[3] In any communicable disease, vaccination is the best primary prevention needed. Likewise for prevention of SARS-CoV-2 scientist worked vigorously to make an effective vaccine.[1] COVID-19 pandemic, a state of apprehensions and anxiety, provided a suitable environment for conspiracies to emerge regarding safety of newly constituted vaccine thereby impeding the control of virus spread and establishment of herd immunity.[6,7]

Surveys held in Portugal and Africa showed more than 50% of respondents being hesitant to COVID-19 vaccine.[8,9] Respondents in this particular study bearing no significant exception to this trend, showed a hesitancy rate of 54.6 %. However, studies conducted in Ireland, United Kingdom and Australia showed a hesitancy rate of less than 50% which may depict difference of vaccine hesitancy in developing and developed countries.[10,11]

With regards to the gender discrepancy towards hesitancy to COVID-19 vaccination, a survey in UK showed that females were predominantly hesitant [12, 13], which poses similarity to this research with greater hesitancy rates of 68.9% in females. Research in Bangladesh shows vaccine hesitancy was more in age groups older than 18 years and amongst low literacy populace.[14] A similar trend is seen in this study where population groups over 28 years exhibited higher hesitancy to COVID-19 vaccination. A study on Iraqi population showed 61.1% willingness to receive COVID-19 booster dose similar to a study held in Pakistan which showed high acceptance rates. However, in this study there were only 15.5 % people who had actually received a booster dose. This is indicative that willingness to get booster dose is not necessarily followed by actually receiving a booster shot.[15]

Many misconceptions and conspiracy theories that lead to vaccine hesitancy in Europe and Middle East[5,13] were also the main reason of hesitancy in this study where the top most were unbeknown side effects and hasty formulation. Many reasons played role in individuals getting vaccinated as shown in the study held in China and UK which showed high acceptance rate if vaccine were to be recommended by friends and family and provided free of charge.[16] In this particular study the top contributory (pulling) factor to get vaccinated was protection of loved ones from acquiring COVID-19

infection.

Limitations

Since this study is being held on a specific population of Pakistan with convenient sampling, it cannot be generalized to whole population and further large-scale studies are needed to confirm findings.

CONCLUSION

It is inferred that there is a decline in hesitancy towards covid-19 vaccination from initial days till date. But still remarkable number of participants are reluctant to get vaccination mostly due to fear of its side effects. With awareness program and focused strategy this can be further reduced; leading to eradication of misconceptions and enhanced vaccine compliance.

Acknowledgments: None

Disclaimer: None

Conflict of Interest: None

Ethical statement: The purpose and procedure of research was fully explained and a written informed consent was taken from all the individuals who participated in the study. Anonymity and confidentiality of the participants was ensured. Moreover, the research was ethically approved by IRB Fazaia Medical College.

Funding Disclosure: None

Supplementary Materials (if any): None

Authors' Contributions:
Dr Faria helped to write down the article and give it a shape with references.

Dr Sumiaya helped to gather data and analyze it.

Dr Ayesha helped to write the discussion and conclusion of the article.

Dr Arshia acted as a supervisor and guiding through everything.

Dr Talha and Madam Javeria helped to collect data and proof read the entire article.

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RESEARCH ARTICLE

CORRELATION OF NEUTROPHIL TO LYMPHOCYTE RATIO AND PLATELET TO LYMPHOCYTE RATIO WITH HIGH RESOLUTION COMPUTED TOMOGRAPHY IN COVID-19 PATIENTS

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ABSTRACT

Objective: *To correlate the Platelet-to-Lymphocyte Ratio (PLR) and Neutrophil-to-Lymphocyte Ratio (NLR) with Computed Tomography Severity Score (CT-SS) in COVID-19 patients.*

Study design: *Cross sectional analytical study.*

Place of study*: Collaborative study between departments of Physiology, Pathology and Radiology at HITEC-IMS.*

Duration of study: *From June 2020 to December 2021.*

Patients and methods: *A total of 83 (N=83) COVID-19 patients were included in the study through Non-Probability Purposive sampling. They were grouped into mild disease(n=44) and severe disease (n= 39) based on their HRCT severity scores. Their blood samples were obtained and NLR and PLR were correlated with CT-SS using the Spearman's correlation.*

Results: *Data were analyzed by SPSS version 25. Both NLR and PLR showed strong positive correlation with the HRCT severity score ($r = 0.471$, $p < 0.05$ for NLR and $r = 0.347$, $p < 0.05$ for PLR). Mann Whitney test scores showed that NLR & PLR were significantly different in both the mild and severe disease groups based on HRCT severity scores ($p< 0.05$).*

Conclusion: *NLR and PLR values could serve as prognostic markers in patients with COVID-19 in place of HRCT.*

Keywords: *COVID-19, CT-SS, HRCT, NLR, Prognostic markers, PLR.*

INTRODUCTION

The novel corona virus outbreak was declared as a global pandemic by WHO on March 11, 2020, which created an urgency to study the diagnostic, treatments and prognostic markers of COVID-19.[1]

Real-Time Reverse Transcription Polymerase Chain Reaction (RT-PCR) is most reliable in diagnosing COVID-19 and is usually performed on nasal swabs.

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Received: 30 Nov 2023; revision received: 28 Dec 2023; accepted: 29 Dec 2023

Different hematological parameters like Blood Complete Picture, C-Reactive Protein (CRP), Erythrocyte Sedimentation Rate (ESR), Serum Ferritin, and Procalcitonin (PCT), and radiological imaging like chest X-ray were used as diagnostic tools for monitoring the progression of lung involvement in COVID-19 disease.[2] Among these, the most effective diagnostic method to detect lung involvement at relatively early stage and estimate the progression of disease from initial diagnosis to discharge from hospital, is Computed tomography (CT) scan.[3]

Chest High Resolution Computed Tomography (HRCT) is a helpful mean in the early discovery and evaluation of disease gravity in COVID-19 patients. There are multiple CT-scoring systems like Total Severity Score (TSS),

Computed Tomography Severity Score (CT-SS) and Computed tomography Score (CTS) to categorize the degree of COVID-19 disease severity. The CT-SS score is a modification of a technique that was first applied in the 2005 SARS pandemic.[3] Lung opacification is used in this scale as a stand-in for lung disease progression. An area of increased attenuation in the lungs, is labelled as Ground Glass Opacity (GGOs). The characteristic radiological pattern of COVID-19 disease is multiple GGOs in the periphery of lungs. . Follow up HRCT can also help in evaluation of disease progression.

The main pathophysiology of COVID-19 revolves around inflammation. The indices of Neutrophil to Lymphocyte Ratio (NLR) and Platelet to Lymphocyte Ratio (PLR) indirectly depicts the inflammatory status of the patient. Recent research has validated NLR and PLR as prognostic markers in number of illnesses, including Acute Respiratory Distress Syndrome (ARDS), malignancies, sepsis, pneumonia and cardiac diseases.[4,5]

Both the NLR and PLR consistently demonstrate greater levels across all observed time points in serious cases of COVID-19. Further, the disparity between NLR and PLR readings becomes wider as the disease severity increases. Both NLR and PLR reflects an increasing trend beginning with admission and culminating at the 7-day point.[6]

For developing countries like Pakistan, where resources are limited and out of reach for most of the patients, CT scan is a costly option. Alternatively, Serial CT scans expose the patients to a very high dose of radiation, which itself is a health hazard. Therefore, there is a need to look for alternatives as prognostic markers for COVID disease which should be safe, cost effective and at the same time as useful as HRCT for predicting prognosis of this disease. For developing countries like Pakistan, where there is dearth of tertiary care facilities lodging CT scan machines, this further limits the patient care.

Purpose of this study was to find correlation between PLR and NLR with HRCT scoring and then establishing these ratios as significant prognostic markers for devising and modifying the treatment plans and discharge criteria in COVID-19 disease patients.

MATERIAL AND METHODS

This was a one and a half year long cross-sectional analytical study conducted from June 2020 to December 2021, after ethical approval from IRB (Ref # HITEC-IRB-29-2022) at Physiology department of HITEC-Institute of Medical Sciences in collaboration with the Pathology and Radiology department of HIT hospital. Sampling technique used was non-probability purposive sampling. The sample size was calculated using the WHO calculator by taking a confidence interval, 80% power of study with an anticipated NLR mean + SD of group I is 3.76+4.5 and group II is 8.44+8.86.[7]

All patients were Covid positive (N=83) both males and females between 18 to 70 years of age.[8] Data were collected retrospectively, in the form of Blood CP and HRCT reports. Blood CP reports were collected from Pathology laboratory of HIT hospital. Blood CP was performed on hematology Analyzer Sysmex (Sysmex Corporation, Kobe, Japan) KX21 3-Part Differential. HRCT severity scores were calculated by using Chest Severity Score System (CT-SS). The method used here was published in Radiol Cardiothoracic imaging and was proposed by Yang et al.in March 2020.[9] The 18 segments of both lungs were divided into 20 regions for this study. The left upper lobe's posterior apical segment was further divided into apical and posterior segmental regions, while the left lower lobe's antero-medial basal segment was split into anterior and basal segmental regions. After wards, the lung opacities were intuitively evaluated on chest CT scan by Radiologist. Depending upon the parenchymal opacification, the regions were scored as 0, 1 or 2 showing involvement of 0%, 1-50% or 51-100% respectively. The overall score ranges from 0-40 depending upon the sum of point scored in all 20 lung segments.[3]

HRCT reports were prepared by consultant radiologist of HIT hospital by using this score. HRCT was performed on Toshiba (Japan) Alexion-16 slice CT scan machine. These patients (N=83) were divided into mild disease group (n=44) with CT-SS of 1-19 and the severe disease group (n=39) with CT-SS of 20-40. PLR was calculated by dividing Absolute Platelets Count APC (150,000-450,000/ul) by Absolute Lymphocyte count ALC (1000-4800/ul).[10] NLR was calculated by dividing Absolute Neutrophils Count ANC (2500-6000/ul) by Absolute Lymphocyte Count ALC (1000-4800/ul) using QxMD calculator.[8,11] Data were analyzed by SPSS version 25 (SPSS Inc., Chicago, IL, USA).

RESULTS

This study included 52 (62.7%) males & 31 (37.3%) females, with an average age of 47.97 years (SD + 13.6). A total of 83 COVID-19 patients were grouped into mild

disease (N=44) with CT-SS 1-19 and in the severe disease group (N=39) with CT-SS 20-40.

We studied the correlation between the Computed Tomography Severity Score (CT-SS) and two inflammatory markers: PLR and NLR.

The median Neutrophil to Lymphocyte Ratio (NLR) was seen to be significantly higher in severe disease group. In the mild disease group having CT-SS between 1-19, it was 2.91 (IQR:1.60 - 4.69), while in the severe disease group having CT-SS between 20-40, the median NLR was 8.00 (IQR: 4.81 -14.67).

The median PLR was seen to be significantly raised in severe disease group. In the mild disease group (CT-SS 1-19), it was 148.67 (IQR: 97.47-251.82), while in the severe disease group (CT-SS 20-40), the median PLR was 210.89 (IQR: 150.0-324.9).

According to the table II, Mann Whitney test scores showed that NLR & PLR were significantly different in both the mild and severe disease groups based on CT-SS ($p< 0.05$) *.

Spearman correlation score was obtained for correlating the HRCT severity score with the inflammatory markers; NLR and PLR. Both showed strong positive correlation with the CT-SS ($r = 0.471$, $p < 0.05$ for NLR and $r = 0.347$, $p < 0.05$ for PLR).

DISCUSSION

According to the findings of this study, COVID-19 pneumonia patients with high HRCT scores had considerably higher NLR and PLR ratios. Explosive and unrestrained production of cytokines is the central pathophysiology of COVID-19 pneumonia.[12]. The virus reaches alveolar cells via Angiotensin Converting Enzyme 2 receptors, prompting the cells to release inflammatory chemicals that activate alveolar macrophages. The stimulation factors and chemokines produced by macrophages trigger an increase in mononuclear cells in lung tissue. The severe consequences of COVID-19 pneumonia are caused by a cytokine storm caused by extreme inflammatory cell infiltration. In our study, the NLR and PLR ratios were significantly higher in the severe illness group.[12,13]

Previous research shows that pneumonic COVID-19 patients had lower lymphocyte, monocyte, and eosinophil counts, as well as greater neutrophil and CRP levels, than non-pneumonic individuals.[14] WBC and their varying quantities, which include lymphocytes, neutrophils, eosinophils, and monocytes, are associated with inflammation and the immune system [12] Platelets, which are anucleate blood cells derived from megakaryocytes in the bone marrow, play an important role in the host's inflammatory and immunological responses, as well as the regulation of hemostasis and thrombosis.[15]

Yang et al. and Sun et al. studied certain haematological indices in COVID-19 patients and discovered that NLR, PLR, and MLR values were significantly higher in severe patients compared to non-severe patients.[15]

Our findings were consistent with previous research on the relationship between NLR and the prognosis of a variety of infectious diseases.[16] The likely explanation for this association is that neutrophils are a constituent of the leukocyte population that activates and travels from the venous system to the immunological organ or system, creating a large number of reactive oxygen species that can cause DNA injury in cells and release the virus. Consequently, antibody-dependent cell mediated cytotoxicity (ADCC) has the property to directly terminate the virus, expose virus antigen, and trigger cell-specific and humoral immunity.[17] Additionally, neutrophils interact with countless additional cell types then yield a widespread array of cytokines and effector chemicals, as well as circulating vascular endothelial growth factor. [16]

One more study found that the absolute value of lymphocytes was significantly lower in the severe ICU group, whereas neutrophil count was significantly more.[18]

In the current study, the HRCT severity score was associated with these inflammatory indicators. Together, these parameters displayed a strong positive association with the HRCT severity score. In COVID-19 patients, PLR has some links with coagulation disturbances, even though it does not have a substantial link with other inflammatory markers in other inflammatory disorders like myocardial infarction.[14]

Ding et al discovered that the NLR index is absolutely correlated with the degree of hospital stay and can forecast illness outcome.[19]

According to Le Qiu et al, in burn patients, NLR was a strong predictor for 3 months mortality.[20] A recent study found that patients with COVID-19 may have a worse prognosis if they have high neutrophil/lymphocyte ratios (NLR) and low lymphocyte/CRP ratios (LCR).[20]

Milena et al, correlated NLR, PLR, and eosinophils with

HRCT severity scores; they included 149 COVID positive patients and 149 healthy age-matched subjects. In our study, we used CT-SS to assess COVID severity and divided our sample population into two groups based on severity scores. In contrast, they divided COVID patients into three groups based on international standards established by the Fleischner Society Glossary of thoracic imaging.

Stage 1, categorized as mild severity including less than three areas of GGOs with a maximum diameter of 3cm. For Stage 2- Moderate severity, the criteria encompass up to three GGOs area or multiple lung areas with GGO linked to a propensity for lung consolidation (<50% lung parenchyma). Stage 3-High severity is categorized by diffuse GGO or lung consolidation covering more than 50% of lung parenchyma, accompanied by signs of distortion of lung architecture. Their results showed median NLR 2.56 (IQR=1.72-3.79) in COVID-19 patients vs 2.11 (IQR=1.65-2.57) in healthy controls. And median PLR 151.85 (IQR=112.86-211.59) in COVID-19 patients vs 125.84 (IQR=99.02-155.36) in healthy controls.[14] They didn't compare median NLR and PLR in three severity groups, as we did in our study. Our results displayed median NLR in mild disease was 2.91 (IQR=1.6-4.69) vs 8.00 (IQR=4.81-14.67) in severe disease and median PLR in mild disease was 148.0 (IQR=97.47-251.82) vs 210.0 (IQR=150.0-324.9) in severe disease.

In 2020 Yang et al, explored the association of NLR with COVID-19 disease severity in five centers of China. They graded the disease severity by symptomatology and imaging (TSS) into mild, moderate and severe disease.[21] Their results are analogous to our study, showing a mean NLR 2.38+1.10 in mild disease, 3.74+1.49 in moderate and 9.26+2.76 in severe disease.

A retrospective study conducted on 100 patients in India in 2021 classified the patients into mild and severe based on their clinical features. Their results showed that PLR was far lesser (141.4+82.9) in mild patients than in severe ones (252.6 +198.8). NLR was also calculated to be 3.76+4.5 in mild disease while it was 8.44+8.8 in severe disease.[7] Our study differed from theirs in that we compared the NLR and PLR ratios with the CT severity score, whereas their study compared these ratios with clinical symptoms.

Not only do NLR and PLR values positively correlate with the severity of COVID-19 disease, but they can also be used as a more practical, safe, and cost-effective, that can take the place of a CT scan to predict severity and influence the treatment plan. Additionally, they can assist the clinician in determining when and if to prescribe a chest CT scan, which can help avoid repeat CT scans.

Limitations of the study

The major limitation in our study was that it were conducted in single center.

CONCLUSION

Overall, our results demonstrate a significant positive correlation between the HRCT severity score and two inflammatory markers, NLR and PLR, in COVID-19 patients.

These findings suggest that elevated NLR and PLR values could serve as an indicator of the systemic inflammatory response seen in COVID patients, as reflected by HRCT severity score. They can be used as prognostic marker for COVID-19 pneumonia in settings where HRCT facilities are not available.

Authors' contributions:

Prof. Dr Farhat Abbas Bhatti, Dr Rabia Waseem Butt, Dr Sumera Mumtaz, Dr Radia Amir: Substantial contributions to the acquisition of data

Dr Sumera Mumtaz: Data entry, Analysis, and interpretation for the work

Dr Sumera Mumtaz, Dr Radia Amir: Drafting the work

Prof. Dr Zubia Razzaq, Prof. Dr Aneeqa Shahid: Reviewing work draft critically for important intellectual content

Prof. Dr Zubia Razzaq: Final approval of the version to be published

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Acknowledgement:

We would like to acknowledge Prof. Dr. Wajiha, In-charge Research Cell, HITEC-IMS for helping in statistical analysis of our study.

Disclaimer:

Conflict of Interest:

The authors of this manuscript declare no relationship with any company, whose products or services may be related to the subject matter of this article.

Ethical statement:

Ethical approval was obtained from ERB of HITEC-IMS.

Funding Disclosure:

The authors received no financial support for the research, authorship, and/or publication of this article.

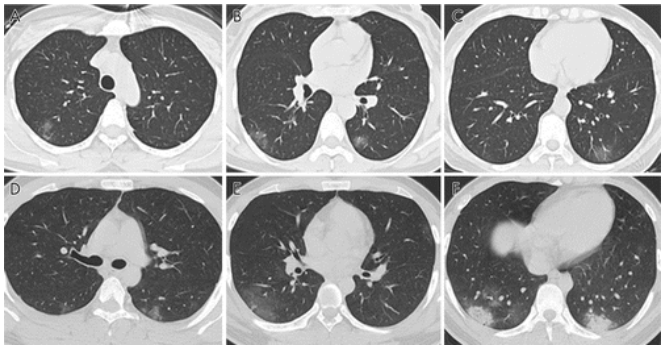

Fig. 1: MILD DISEASE: Faint glass opacities and sporadic consolidation signifying mild COVID disease.

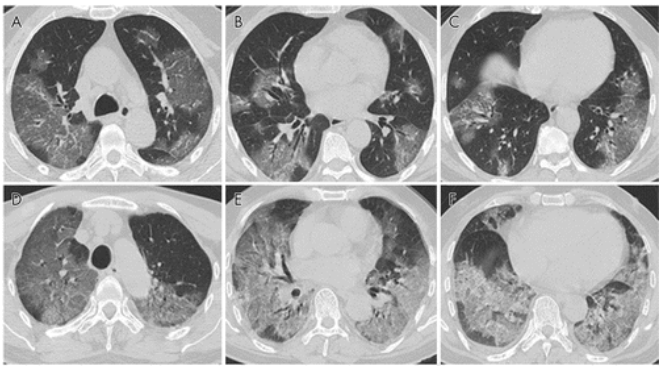

Fig. 2: SEVERE DISEASE: Dense areas of consolidation (GGOs) involving major lung parenchyma signifying severe COVID disease.

Table I: Median NLR & PLR for mild & severe COVID disease.

Parameter		Mild Disease (CT-SS 1-19)	Severe Disease (CT-SS 20-40)
NLR	Median	2.91	8.00
	IQR	1.6-4.69	4.81-14.67
PLR	Median	148.67	210.89
	IQR	97.47-251.82	150.0-324.9

Table II: Comparison of NLR & PLR in mild and severe disease using Mann Whitney Test.

Ratios	Groups	Total Number (N)	Mean rank	Sum of Ranks	*p*-Value
NLR	Mild Disease (CT-SS 1-19)	44	31.03	1365.5	0.000*
	Severe Disease (CT-SS 20-40)	39	54.37	2120.5	
PLR	Mild Disease (CT-SS 1-19)	44	34.43	1515.0	0.002*
	Severe Disease (CT-SS 20-40)	39	50.54	1971.0	

*p-value less than 0.05 is considered significant

Table III: Spearman's correlation between CT-SS and NLR & PLR (N=83)

			PLR	NLR	CT-SS
Spearman's rho	PLR	Correlation Coefficient	1.000	0.729	0.347
		Significance (2-tailed)	-	0.000	0.001
	NLR	Correlation Coefficient	0.729	1.000	0.471
		Significance (2-tailed)	0.000	-	0.000
	CT-SS	Correlation Coefficient	0.347	0.471	1.000
		Significance (2-tailed)	0.001	0.001	-

RESEARCH ARTICLE

UNLOCKING HEPATITIS B AND C INSIGHTS: EXPLORATION OF RISK AWARENESS AMONG UNIVERSITY STUDENTS IN THE CAPITAL TWIN CITIES OF PAKISTAN

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ABSTRACT

Background: *Pakistan, a developing nation, grapples with a growing burden of Hepatitis B and C, exerting a substantial strain on the country's economy. Mitigating this challenge necessitates a robust strategy emphasizing prevention of infection by hepatitis B and C viruses.*

Objective: *This study aimed to assess awareness among university students in the capital twin cities of Pakistan regarding Hepatitis B/C, encompassing knowledge about risk factors, vaccination, and treatment options.*

Methods: *This cross-sectional survey was conducted from January 2023 to June 2023 in Rawalpindi and Islamabad, this research involved interviewing 1008 students from eight diverse universities. The main emphasis was on identifying areas that required intervention to mitigate the future impact of Hepatitis B and C in Pakistan.*

Results: *Out of 1008 students, 57.5% were identified having Hepatitis B/C as viral diseases, and 74% recognized their impact on the liver. However, only 28% were aware that these viruses could be transmitted through dental instruments and ear/nose piercing. Additionally, 38% believed transmission could occur through blood/blood products and the reuse of razors. While 56% had encountered hepatitis-related advertisements, a mere 11.6% of social science students had received the HBV vaccine.*

Conclusion: *While a majority of participants possessed a fundamental understanding of Hepatitis B/C as viral diseases affecting the liver, awareness regarding key risk factors for viral transmission was notably lacking. Urgent, extensive awareness programs are imperative to educate the populace on these risk factors. Moreover, local production of the HBV vaccine is essential to mitigate costs. A fundamental change in the mindset of both patients and doctors is essential to reduce the unnecessary use of injections.*

Keywords: *Awareness among Students, Hepatitis B Virus, Hepatitis C Virus, Pakistan, Risk factors*

INTRODUCTION

Hepatitis B and C present substantial threats, giving rise to severe liver conditions such as hepatocellular carcinoma, cirrhosis, and end-stage liver disease. Worldwide, an estimated 350 million individuals live with Hepatitis B, and another 200 million are affected by Hepatitis C.[1,2] World Health Organization reported 308,000 annual deaths due to liver cancer and 785,000 due to cirrhosis.[3] In Pakistan, the Hepatitis B virus has a prevalence ranging from 3% to 4%, and the Hepatitis C virus is prevalent at 5%. The country, with a population of 185 million, faces increasing virus prevalence due to various factors, including the reuse of syringes, needles

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Received: 22 Nov 2023; revision received: 22 Dec 2023; accepted: 29 Dec 2023

for piercing, drug use, tattooing, inadequate implementation of blood transfusion standards, and unsterilized medical instruments.[2,4]

The treatment for viral hepatitis is costly, imposing a substantial economic burden on Pakistan.[5,6] Prevention emerges as the primary defense against this epidemic. While initiatives by the Ministry of Health and the World Hepatitis Alliance aim to raise awareness through media, the focus should be on identifying target areas for effective health education.[2]

Within the Pakistani population, there exists a moderate knowledge about HBV and HCV infections, yet awareness of the associated risk factors remains limited.[2,7] Previous surveys indicate varied awareness levels; for instance, in Karachi, 61% recognized HCV as a viral disease, 49% believed in needle transmission, 5.3% linked it to ear/nose piercing, and 20.6% knew about its cancer-causing potential.[7,8,9] Another study in 2006 reported only 19% HCV awareness among injection drug users in Quetta and Lahore. Educational backgrounds significantly influenced knowledge about HCV infection.[10,11] This study aimed to assess the understanding of risk factors, vaccination, and treatment options concerning Hepatitis B and C among university students in the twin cities of Pakistan's capital. The survey encompassed 1008 students from eight universities, representing various academic disciplines.

MATERIALS AND METHODS

The study, approved by the Ethical Review Committee of the International Center of Medical Sciences Research (ICMSR), took place in Rawalpindi and Islamabad, with a combined population exceeding 4.5 million and a literacy rate exceeding 70%. A structured questionnaire in English was designed, covering personal information and awareness, risk factors, vaccination, and treatment preferences regarding Hepatitis B and C. Data were collected through random sampling and analyzed using Microsoft Excel and SPSS 12.

RESULTS

Of the 1025 survey responses, 13 were excluded, resulting in 1008 completed surveys for analysis. Respondents represented Bachelors (57.8%), Masters (40%), and Doctoral (2.2%) programs across eight disciplines. The data, organized by academic discipline, unveiled diverse levels of awareness about HBV and HCV, including knowledge of risk factors and treatment options, as outlined in Table I.

Table I: Understanding of Hepatitis B and Hepatitis C Awareness, Risk Factors, and Treatment Options Among University Students.

Knowledge of HBV/HCV and Associated Factors	Data Acquisition	No.	% age
Hepatitis B and C are illnesses resulting from which of the followings?	Bacteria	204	20.2
	Fungus	30	3.0
	Virus	582	57.5
	No Idea	196	19.4
Hepatitis B and C primarily impact which organ?	Brain	16	1.6
	Heart	21	2.1
	Liver	749	74.0
	Stomach	78	7.7
	No Idea	145	14.3
	All	3	0.3
Can Hepatitis B and C be transmitted by individuals who appear healthy?	It can spread	590	58.3
	It can`t spread	281	27.8
	No Idea	141	13.9

Modes of transmission for Hepatitis B and C include:	Contaminated drinking water	278	27.5
	Blood and Blood products	386	38.1
	Reuse of razor at barber`s shop	387	38.2
	Needles use for ear and nose piercing	289	28.6
	Unhygienic food	165	16.3
	Dental Instruments	293	28.9
	Unprotected Commercial sex	316	31.2
	No Idea	10	1.0
	All of these	159	15.7
Can Hepatitis B and C be transmitted through the consumption of food from individuals with HBV or HCV?	It can spread	283	28.0
	It can`t spread	604	59.7
	No Idea	125	12.3
Have you ever encountered advertisements related to Hepatitis?	Yes	570	56.3
	No	325	32.1
	No Idea	117	11.6
Can Hepatitis B and C lead to cancer?	Yes It can cause cancer	359	35.5
	No cancer is different disease	647	63.9
	No Idea	6	0.6
Are there any available treatments for patients with Hepatitis B and C?	Yes	791	78.2
	No	76	7.5
	No Idea	145	14.3

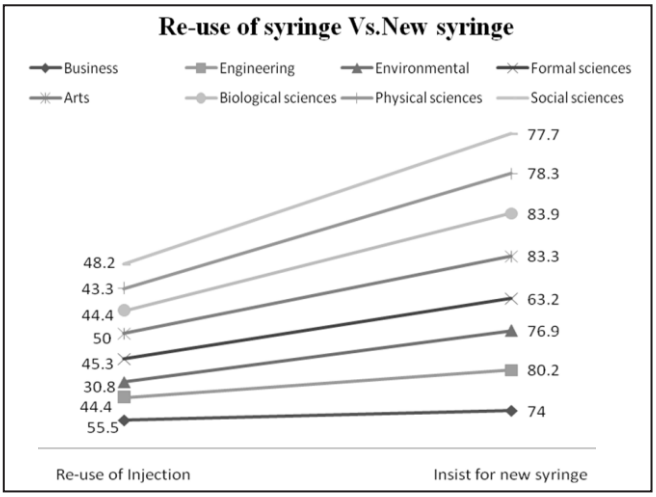


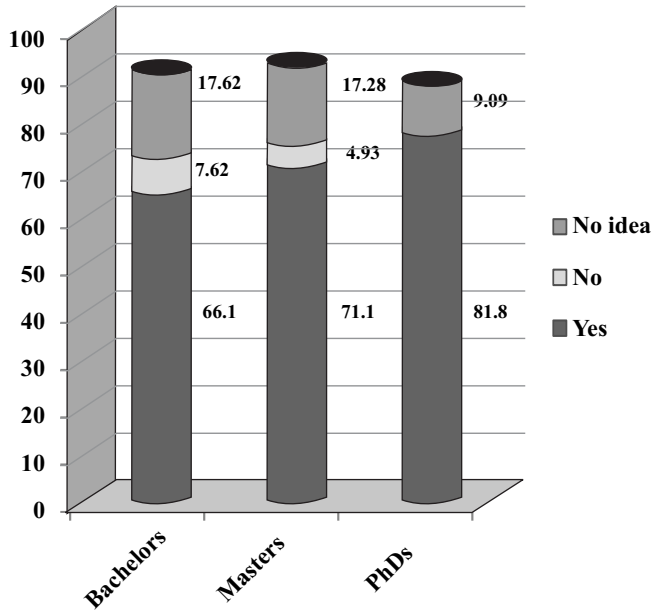
Figure 1: A Comparative Insight into Students' Perceptions Across Disciplines Regarding HBV/HCV Transmission via Reused Injection Syringes and Their Preference for New Syringes During Injections.

Merely 57.5% of the university-going population recognizes Hepatitis B and C as viral diseases, with an additional 20% mistakenly attributing their origin to bacteria. A noteworthy 74% acknowledge the liver as the target organ, yet 58% believe transmission can occur even from individuals appearing healthy. Awareness concerning transmission modes remains deficient; a mere 38% are aware of blood/blood products and razor reuse by barbers as potential transfer mediums for HBV/HCV. Moreover, 29% associate transmission with the reuse of needles for ear/nose piercing and dental instruments. A comprehensive 35% grasp the cancer-causing potential, while 56% have encountered advertisements on HBV/HCV awareness.

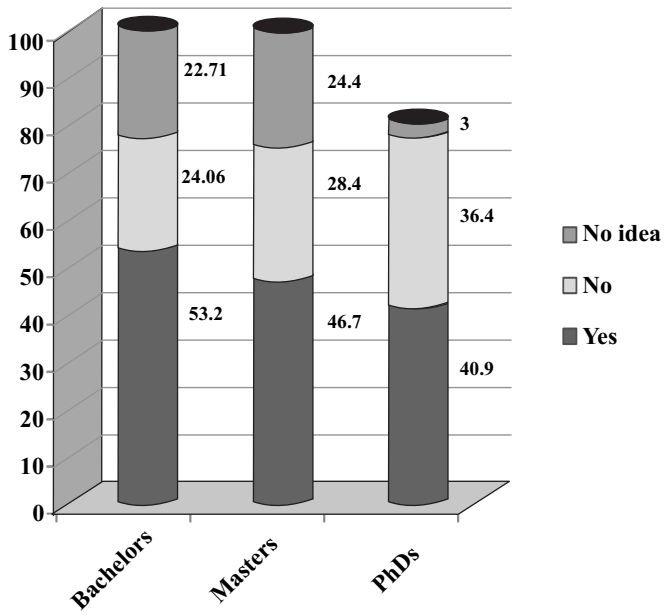
In Figure 1, a comparative analysis reveals students' perspectives across disciplines on HBV/C transmission via reused injection syringes and their insistence on new syringes during injections. Notably, 30.8% of Environmental Sciences students and 55.5% of Business Studies students perceive the risk of transmission through reused syringes, whereas 63.2% of Formal Sciences and an overwhelming 83.9% of Biological

Sciences students insist on new syringes during injections.

In Figure 2, it is evident that 66% of Bachelor's, 71% of Master's, and 81% of Doctoral students believe that a Hepatitis B vaccine is accessible. Conversely, 53% of Bachelor's, 47% of Master's, and 41% of Doctoral students hold the belief that a vaccine for Hepatitis C virus is available.



Hepatitis B



Hepatitis C

Figure 2: Perception of Hepatitis B and C Vaccine Availability Among Students in Various Degree Programs.

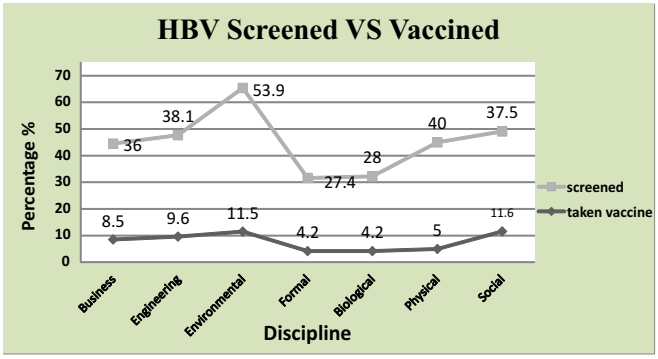


Figure 3: Participants across Disciplines - Screening for Hepatitis B Virus vs. Hepatitis B Vaccine Uptake.

Figure 3: Comparative Analysis of Participants Across Disciplines, highlighting that 27% of Formal Sciences and 54% of Environmental Sciences students have undergone screening for the Hepatitis B virus. Furthermore, 4.2% of Formal Sciences/Biological Sciences students and 12% from Environmental/Social Sciences have received the Hepatitis B virus vaccine.

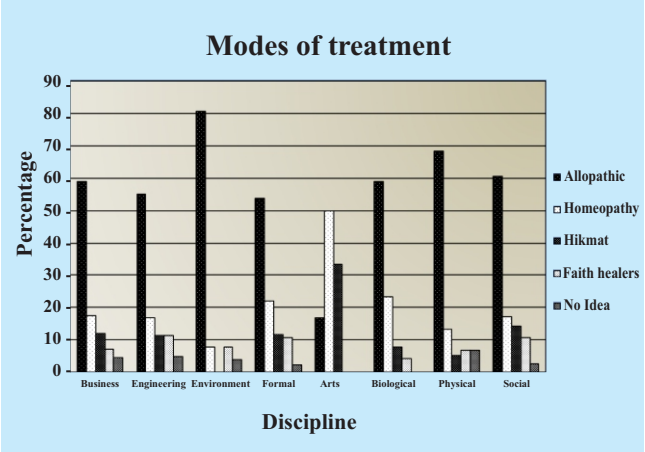


Figure 4: Perspectives on Optimal Treatment for Hepatitis B/C among Students from Diverse Disciplines.

Figure 4: Diverse Perspectives on Hepatitis B/C Treatment Options Among Different Disciplines. Notably, 81% of Environmental Sciences students prefer Allopathy, while 50% and 33% of Arts students endorse Homeopathy and Hikmat, respectively, as illustrated.

DISCUSSION

Concerning transmission awareness, 58.3% believed HBV/HCV could be transmitted by asymptomatic individuals, contrasting with 45.7% among barbers. Additionally, 35.5% associated these viruses with cancer, a higher awareness than observed in the barber community (26.6%). Key gaps in knowledge emerged, with only 38% and 29% acknowledging blood/blood

products and dental instruments as potential transmission routes.[18,14] Notably, misconceptions persisted, with some associating HBV/HCV transmission with contaminated water and unhygienic food.

Pakistan's high injection rate, with 94.2% deemed unnecessary, highlights a concerning issue. Misguided beliefs about syringe reuse were evident, with 30.8% of environmental sciences and 55.5% of business students associating HBV/HCV transmission with reused syringes.[14,15] Efforts to decrease unnecessary injections are crucial, as evidenced by the preference for injectable medicines, particularly if equally effective as oral alternatives. A shift in both doctor and patient perspectives is essential to reduce unnecessary syringe use, especially given the reported involvement of certain groups in repackaging unsterilized syringes.[15,16,17]

Despite global success stories in hepatitis reduction through targeted interventions and vaccination, this study underscores a significant lack of awareness in Pakistan.[14] A mere 11.6% of social science students reported HBV vaccination, reflecting a need for expanded programs targeting adult populations to alleviate future burdens.[18,19] Divergent opinions on treatment options were noted, with allopathic medicine favored by the majority, while a notable percentage believed in faith healers' interventions.

This study sought to assess awareness, risk understanding, and perceptions of vaccination and treatment options for Hepatitis B/C among university students in the capital twin cities of Pakistan. Notably, 57.5% of participants identified HBV/HCV as viral diseases, surpassing the awareness reported among barbers in a previous study (39.6%). Similarly, 74% recognized the primary impact on the liver, a higher percentage than in young individuals applying for military recruitment (56.5%).[1,7]

CONCLUSION

Amidst the rising prevalence of viral infections, this study illuminates the awareness levels of hepatitis within the highly educated community residing in the capital twin cities of Pakistan.[10,19] There was a noticeable lack of awareness regarding significant risk factors, including misconceptions about transmission through water and food.

Given the economic challenges associated with hepatitis treatment in a developing country like Pakistan, immediate efforts are imperative to boost awareness and rectify misconceptions. The study underscores the urgency of targeted educational campaigns and the expansion of vaccination programs to alleviate the imminent burden of hepatitis B/C on the population.

Authors Contribution

Seneen Noor: Conception of study / Designing / Planning, Experimentation/Study Conduction, Manuscript Writing, Critical Review

Elyeen Noor: Manuscript Writing, Experimentation/Study Conduction, Critical Review, Facilitated for Reagents/ Material Analysis

Rizwan Uppal: Conception of study / Designing / Planning, Manuscript Writing, Facilitated for Reagents/ Material Analysis

Zahra Zahid Piracha: Conception of study / Designing / Planning, Experimentation/Study Conduction, Analysis/ Interpretation/Discussion, Critical Review, Manuscript Writing, Facilitated for Reagents/ Material Analysis

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RESEARCH ARTICLE

TREATMENT OF FEMALE PATIENTS WITH INHERITED BLEEDING DISORDERS IN REPRODUCTIVE AGE: A SINGLE CENTRE STUDY FROM NORTHERN PAKISTAN

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ABSTRACT

Introduction: *Inherited bleedings disorders (IBD) in women are mismanaged in Pakistan due to lack of standardized treatment options. The most common is Von Willibrand Disease (VWD) followed by rare bleeding disorders (RBD). Heavy menstrual bleeding (HMB) and postpartum hemorrhage (PPH) are the main clinical manifestations causing lot of morbidity and mortality.*

Objective: *To document current treatment practices in female patients in reproductive age with IBD.*

Study Design: *A retrospective study with analysis of patients' records from Hemophilia Treatment Centre (HTC) Rawalpindi.*

Duration: *June 2017 – June 2022*

Place: *HTC, Haemophilia Patient Welfare Society, Rawalpindi.*

Patients and Methods: *Female patients with IBD aged between 11-45 years were included in study. VWD, RBD like deficiencies of factors (I, II, V, VII, X, XI, XIII) and Platelet Function Disorders e.g. Glanzman Thrombesthenia (GTT) and Bernard Soulier Syndrome (BSS) as well as Hemophilia carriers. HMB and PPH were documented along with treatment given.*

Results: *Total 67 patients were included. Age of Menarche was between 11 to 15 years. 89.4% patients with VWD, 60% with RBD and 100% with platelet function defects had HMB. Antifibrinolytic agent was the most common treatment followed by FFP infusion (70 – 86%). Factor replacement was done in 57.5% and OCPs were used in 50% patients. Eleven patients conceived, 10 had full term deliveries and 5 had PPH. They received antifibrinolytics, FFP and factor concentrates*

Conclusion: *In our centre, antifibrinolytics were the most common treatment followed by FFPs, OCPs, hormones and factor concentrates.*

Keywords: *Female patients with IBD in reproductive age, VWD, RBD, Platelet functions defects*

INTRODUCTION

Inherited bleeding disorders (IBD) are a very serious health care issue with lot of morbidity and mortality due to lack of awareness. Inherited Bleeding Disorders are seen in men as well as women. Hemophilia A & B (Factor VIII & IX deficiency) is the most common disorder in males but in women Von Willebrand Disease (VWD) is the commonest.[1] VWD is caused due to deficiency of or abnormality of VWF present in blood,

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which is essential for platelet plug formation. VWF also protects factor VIII in circulation, so its deficiency or absence results in decreased levels of factor VIII. VWD is an autosomal disorder, thus affecting both men and women. There are three types of VWD. Type I and Type II have a autosomal dominant mode of inheritance and are generally mild or moderate in clinical behavior. The most severe form is Type III which is autosomal recessive. Mucocutaneous bleeds are the predominant symptoms but in Type III tissue or joint bleeds may be seen.[1-12] This is the commonest type in Pakistan due to consanguineous marriages.[2] It is very important to correctly diagnose VWD so that appropriate management can be done.

Rare Bleeding Disorders (RBD), are characterized by systemic deficiency of coagulation factors I, II, V, VII, X, XI, and XIII. These disorders are autosomal recessive, therefore due to increased incidence of cousin marriages in our society these disorders are more common here as compared with the west.[2,3] Platelet function disorders like Glanzman Thrombesthenia (GT) and Bernard Soulier Syndrome (BSS) are also seen relatively more frequently here due to the same reason.[4]

Hemophilia is the most well-known and better treated[5] disease which is X-linked and seen in boys mostly.[6] Hemophilia is rare in women. However women who are carriers of factor VIII and factor IX may have varying degrees of bleeding tendency according to the level of factor VIII and IX in them. This has recently lead to categorizing them into a carrier, symptomatic carrier as well as mild, moderate and severe hemophiliacs.[7]

Gene therapy is the latest treatment modality approved for factor IX and VIII and has a considerable impact on the life style of these patient. Although availability to all and morbidity due to viral vector are problems yet to be overcome, it holds a lot of promise to improve the life expectancy of hemophiliacs[8,9] Gene therapy for VWF factor is not available.

The development of treatment of IBDs has made a remarkable improvement in the Quality of Life (QOL) in these patients. Replacement therapy of the missing factor whether human derived or recombinant was a major breakthrough in management of these patients. Availability of factor replacement for treatment of VWD in the developed world plays an important role in improving lives of these patients.[10]

In Pakistan replacement therapy for VWD and other RBD is not readily available so these patients suffers a lot of morbidity and mortality. The mainstay of treatment remains use of blood products like FFP and cryoprecipitate, if available. Adjunctive treatment like antifibrinolytic agent (Tranexamic Acid) as well as oral contraceptive pills (OCP) or hormone based treatment in case of menorrhagia are used mostly.

This study aims to record and categorize the existing state of treatment modalities offered in our clinical setup.

PATIENT AND METHODS

The study was carried out at Haemophilia Treatment Centre (HTC), Haemophilia Patient Welfare Society, Rawalpindi, Pakistan, from June 2017 to June 2022.

Selection Criteria:

Female patients with IBD in age ranged from 11-45 yrs. These include VWD, RBD, (deficiency of factors I, II, V, VII, X, XI, XIII) and functional platelet disorder, Glanzman Thrombasthenia (GTT) and Bernard Soulier Syndrome (BSS).

Age of menarche, treatment modalities in HMB and PPH were recorded after taking proper approval from institutional ethical review board.

RESULTS

This study consisted of total 67 patients having age of menarche between 11-15 years. The breakdown of diagnosis is shown in Fig1. VWD is the most common disease in this group.

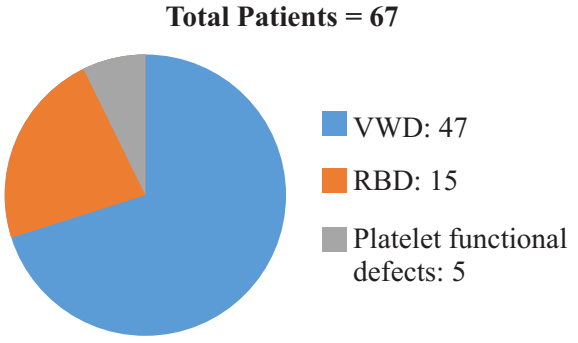

Figure 1: Distribution of patients in three main groups of Bleeding Disorders in Women.

VWD (Von Willibrand Disease), RBD (Rare Bleeding Disorders)

89.4% patients with VWD, 60% having RBD, and 100% with functional platelet disorder reported with heavy menstrual bleeding (HMB).

These patients were managed at the HTC using multiple treatment options available. Antifibrinolytic agent i.e.

Table I: The different treatment modalities used in our patients for HMB. Received 'R', Not Received 'NR'. OCP (Oral Contraceptive Pill), FFP (Fresh Frozen Plasma)

DISEASE	TOTAL PATIENTS	TREATMENT RECEIVED									
		Antifibrinolytics		OCPs/Hormones		FFP		Factor Concentrates		Platelets	
		R%	NR%	R%	NR%	R%	NR %	R%	NR %	R%	NR %
VWD	47	91.5	8.5	57.5	42.5	70.2	29.8	57.5	42.5	-	-
RBD	15	60	40	40	60	86.6	13.4	-	-	-	-
Platelet functional defects	5	100	0	40	60	-	-	-	-	40	60

tranexamic acid was the mainstay of treatment followed by FFP infusion in more serious bleeds. Factor replacement was done in 57.5% patients only. OCPs were used in nearly half the patients. Table I shows the details of treatment in our patients.

Outcome of Pregnancy

Total of 11 patients conceived, 5 patients had PPH and 4 delivered without any complication among total of 9 patients having VWD. There were 2 patients having RBD who conceived without any complaint of PPH. One patient had abortion in previous pregnancy in first trimester. Factor concentrate, antifibrinolytic agent and blood products were administered to these patients. They were delivered in Govt Hospitals (PIMS, BBH). Treatment plan was given by HTC. These patients received factor concentrates, blood products (FFP and Cryoprecipitate) and transmine. Table II gives details of Pregnancy Outcome in this study.

Table II: Pregnancy outcome in eleven patients.

PPH (Post-Partum Hemorrhage)

	Number of patients	PPH	Abortion	Normal Delivery
VWD	9	5	Nil	4
RBD	2	0	1	2

DISCUSSION:

The spectrum of inherited bleeding disorders in women reveals VWD to be the commonest [11] followed by Rare Bleeding Disorders (RBD) which are deficiencies of factors I, II, V, VII, X, XI, XIII. These disorders are mostly autosomal recessive and, thus higher incidence of these disorders in some ethnic groups is seen due to cousin marriages.[2,12]

The clinical signs and symptoms due to bleeding are similar in men and women with addition of menstrual blood loss and excessive bleeding during childbirth in women. HMB is important cause of morbidity impacting the lives of young girls causing psychosocial issues. The incidence of post-partum haemorrhage (PPH) is high in these women, causing increased morbidity and even mortality if not properly managed.[12]

Hemophilia is the most well managed bleeding disorder. For both hemophilia A and B, Factor Replacement Therapy, plasma derived and recombinant coagulation factor concentrate (CFC), is available. Novel therapies like emicizumab and gene therapy are also available now making the lives of hemophiliac fairly comfortable. Hemophilia carriers, who are women have varying degree of bleeding symptoms according to their levels.[7] Treatment of VWD in the west has improved Patients Quality of Life.[10-13]

There is a limited experience of treatment of female patients with VWD and RBD in Pakistan due to lack of awareness and poor facilities. Recommendations for treatments of women affected with these disorders are available for guidance and reference.[10]

In rare Bleeding Disorders the recommended treatment is replacement of the missing coagulation factor. However, in case of minor bleeds using adjuvants like antifibrinolytic only can be effective to control bleeding.[14]

Specific recombinant therapy is available for factor VII and factor XIII in the west whereas no specific factor replacement therapy is available for FII and FV deficiency.[14]

In Pakistan only factor VII concentrates are available but

are very expensive so not affordable. Therefore the mainstay of treatment is use of fresh frozen plasma or cryoprecipitate as appropriate. Our study shows use of FFP in 70 – 86% patients as CFCs are not freely available.

A very useful adjuvant to specific factor replacement therapy is antifibrinolytic like tranexamic acid. Mild Bleeding symptoms are usually controlled by conservative measures like use of ice packs, compression bandage elevation of limb, rest (RICE) and addition of transmine.[15] Our study shows use of transamine in 60 – 100 % patients to control bleeding.

The use of oral contraceptive pills (OCPs) is an effective way of managing menorrhagia. This is used in young women to stop menstrual cycles and thus control HMB by continuous uninterrupted use of OCP.[11,12 &15]

The number of female patients with platelet functional defects like GTT and BSS is very low. The mainstay of treatment was platelet transfusion (40%) and transamine (100%) .[4]

We have a very limited experience of dealing with pregnancies in women with IBD. Our study identified eleven patients who conceived. The results of delivery show relatively better outcomes. This shows the importance of identifying these patients so that they are guided and supported during pregnancy and puerperium.

However, the lack of awareness and diagnostic facilities for bleeding disorders results in adverse outcomes of pregnancies or maternal fatalities due to mismanaged PPH.

CONCLUSION

Antifibrinolytics, FFPs and hormones are the primary treatment in our clinical facility followed by factor concentrate, which are not freely available.

Conflict of interest:

None

Acknowledgement

We acknowledge the contribution of our staff in typing and formatting of the manuscript:-

Mr. Aslam Khan

Mr. Qasim Abbas

Mr. Naeem Ur Rehman

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Tahira Zafar: Critical Review

Maryam Ahmad: Analysis / Interpretation / Discussion, Facilitated for Reagents / Material Analysis

Bilquis Sohail: Experimentation / Study Conduction, Data Collection

Amna Waheed: Experimentation / Study Conduction, Arranging References

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