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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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The *Journal of Shifa Tameer-e-Millat University (JSTMU)* is an open access bi-annually peer reviewed medical journal of the Shifa Tameer-e-Millat University (STMU), Islamabad, Pakistan. The journal encompasses papers from biomedical research, clinical specialties and interdisciplinary medical fields; thereby entertaining the scientific, research and clinical work of a wide variety of health care professionals such as medical practitioners, surgeons, nurses, pharmacists, medical technicians, paramedics, laboratory scientists, physiotherapists, dietitians and bioengineers. The journal is premised on creating influence on the academic as well as corporate thinkers. It is dedicated to presenting advances in medical sciences supporting the recognition and publication of medical scientific research and its effects on human health and well-being. A key question we apply to submission is, "Is this paper going to help readers better understand and conceptualize the research topic while adding something new and innovative to the current pool of knowledge?"

CONTACT

Editor; The Journal of Shifa Tameer-e-Millat University (JSTMU)
Shifa Tameer-e-Millat University, Gate No. 1
Pitras Bukhari Road, Sector H-8/4
Islamabad, Pakistan.

Tel: +92-51-843-8056, Fax: +92-843-8067
e-mail: editor@j.stmu.edu.pk | m.editor@j.stmu.edu.pk
website: https://j.stmu.edu.pk

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EDITORIAL

Upholding the responsible conduct of medical research in Pakistan: The buck stops where?

Akhtar Sherin[1*]

[1] Professor, Khyber Medical University, Institute of Medical Sciences, DHQ Teaching Hospital, KDA Kohat, Pakistan

Correspondence
Akhtar Sherin
akhtarsherin@yahoo.com

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Keywords: *Research Integrity, Scientific Misconduct, Clinical Trials, Research Ethics Committees*

The clinical research landscape in developing countries continues to evolve and grow. The research output of low- and middle-income countries (LMICs) is further enhanced by international collaboration with the developed world. Lower costs, faster recruitment rate and relative ease in marketing approval are the main attractions for the global migration of clinical trials to LMICs.[1] Like other LMICs, Pakistan has made significant progress in mounting research output, specifically clinical research.[2, 3]

The Food and Drug Administration (FDA) of the United States does accept data from foreign studies conducted under the *investigational new drug* application, given that these studies meet the specific criteria outlined by the FDA. Regrettably, clinical research conducted in LMICs often faces challenges in gaining acceptance in the developed world.[4] Main areas of concern are related to ethical lapses in the research conduct, lack of consistency and trustworthiness of the data and methods, failure to follow the investigational plan and poor reporting of adverse drug reactions.[5] This lack of trust and confidence in research from LMICs is raising grave concerns about the equitable distribution of research benefits in terms of the availability of newly approved drugs among developed and less developed countries.[6]

To enhance the global acceptability of our local clinical research, we need to foster research integrity in Pakistan. Pakistan's leading clinical research stakeholders include regulatory bodies, healthcare institutions, hospitals and researchers. The Drug Regulatory Authority of Pakistan (DRAP) is the central body to regulate and oversees clinical research activities in the country.[7] Pakistan Medical and Dental Council (PMDC), primarily a licensing organization, indirectly influenced medical research by setting standards and guidelines for medical research and ethics in medical institutions.[8] Higher Education Commission (HEC) is a regulatory and funding body. It is vital to advance research and innovation in various clinical fields by supporting researchers and capacity building in Pakistan's higher education institutions, universities and research centres.[9] College of Physicians and Surgeons of Pakistan (CPSP) supports and promotes clinical research by including mandatory clinical research for postgraduate trainees and provides research methodology workshops and evaluation of protocols during fellowship training programs.10 Healthcare institutions, hospitals, research supervisors and researchers are the other critical stakeholders responsible for maintaining the utmost scientific rigor and ethical oversight of clinical research.

Earning a global reputation and achieving credibility in clinical research in Pakistan needs consistent and collaborative efforts to ensure ethical practices, adherence to the regulations, and the maintenance of high standards in conducting clinical research. This can be achieved by developing a culture of responsible conduct of research in our institutions and promoting the professional integrity of our researchers. Our primary stakeholders, like DRAP, PMDC, HEC & CPSP, are responsible for developing, disseminating and implementing clear guidelines, policies, and codes of conduct specific to clinical research in

Pakistan. Research institutions must establish research integrity offices for facilitating, monitoring and auditing research activities to ensure compliance with ethical standards and research integrity principles.[11] CPSP, the premier institution responsible for training future clinical researchers, contributes a lot to the training and supervision of clinical research. However, CPSP has to take essential steps for monitoring and auditing its trainees' research projects through supervisors and accredited teaching institutions. The role of supervisors and mentors is very critical, and they should take the responsibility of providing training and guidance to their trainees regarding research integrity by active engagement and monitoring of the research projects.[12] Research Ethics Committees need the special attention of DRAP and all other stakeholders to safeguard the research participants' health and rights and monitor adherence to the approved research protocol.

Institutions like HEC, CPSP, medical colleges and teaching hospitals must provide comprehensive training, education and professional development programs for clinical researchers. Recent progress in the establishment of clinical trials units along with collaboration with the Association of Pakistani Physicians of North America (APPNA) in the form of APPNA-MERIT, the start of the master program in bioethics and certificate courses in clinical trials and good clinical practice are very positive steps for the of clinical research landscape of Pakistan.[13] The prospects of clinical research in Pakistan and its credibility at the international level are up-and-coming. Pakistan has a growing healthcare infrastructure, a large population, and a diverse range of diseases and health-related challenges, which create ample opportunities for conducting impactful clinical research.

Overall, this is the collective responsibility of all stakeholders, including DRAP, PMDC, CPSP, healthcare institutions, hospitals, research supervisors and researchers, to promote responsible conduct in Pakistan's medical research and escalate the credibility of our clinical study globally.

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ORIGINAL ARTICLE

Neophyte baccalaureate nursing student's perceptions of motivation towards clinical practice

Aisha Parveen[1*], Khairunnisa Aziz Dhamani[2], Lubna Ghazal[3], Aurang Zeb[4]

[1] Principal, Assistant Professor, Department of Nursing, Horizon Institute of Health Sciences, Hassanabdal, Pakistan

[2] Professor, Shifa College of Nursing, Shifa Tameer-e-Millat University, Islamabad, Pakistan

[3] Assistant Professor, Department of Nursing, Aga Khan University, Karachi, Pakistan

[4] Associate Professor, Department of Nursing, Rehman College of Nursing Hayatabad, Peshawar, Pakistan

Author's Contribution

[1] Conception, designing, data collection and Article writing

[2] Designing, Supervision, Critical analysis and Review

[3] Supervision, Critical Analysis and Review

[4] Supervision, Critical Analysis and Review

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Correspondence

Aisha Parveen

aishi2007@gmail.com

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A B S T R A C T

Background: Clinical learning is challenging for the initial years of nursing students. They need the motivation to achieve the desired academic outcomes. However, they are likelier to leave the profession due to non-conducive learning experiences during clinical practice.

Methodology: A qualitative descriptive study design was used to explore the neophyte nursing students' perceptions of motivation regarding clinical practice. A total of nine second-year nursing students were recruited through purposive sampling. Individual in-depth interviews were conducted. Data were analyzed through an inductive approach.

Results: The theme that emerged from the study was factors in influencing neophyte's clinical motivation, and the five categories were: the worthiness of clinical practice, range of emotions, clinical environment, clinical educators' roles and characteristics, and personal drive for clinical practice.

Conclusion: The neophyte nursing students' demotivation affects clinical learning. Therefore, providing them with opportunities to practice skills under supervision, giving constructive feedback, and respecting them will enhance their motivation.

Keywords: *Motivation, Clinical motivation, Neophyte nursing students, Factors affecting motivation, Clinical*

Introduction

Motivation is an inner power that can help initiate and perform any task to fulfil the desired outcome. [1, 2] Also, motivated students are open to learning and successful in their academic and work performance. [3, 4] In nursing education, clinical practice is crucial as it helps future nurses enhance their knowledge, attitude, and skills. Moreover, students' clinical practice is a significant aspect of learning about their patients and getting directly involved in patient care. [5] If students are motivated for clinical practice, this may improve the quality of nursing care. [4, 6] In clinical education, the lack of nursing students' motivation challenge educators as students' performance deteriorates, and later on, these students may not act as knowledgeable nurses. [7, 8] In addition, few students decide to quit the program or change their field after graduation[8]. Several factors appear to demotivate nursing students about their profession. These factors are lack of awareness about the nursing profession, selecting the profession under pressure, an unfamiliar environment of clinical site, the stress of clinical teacher, nurses' lack of involvement in decision making, high workload and lack of respect, and lower social status of the nursing profession. [8, 9] In

Pakistan, more than 50% of decisions for admission in nursing are taken by parents, which can also impact the motivation of students. [10] Though adequate research has been done on students' academic motivation, there is limited work in the context of clinical motivation in neophytes in nursing education. Most studies in nursing education on motivation have mainly focused on the relationship between a students' clinical learning environment and motivation to become a nurse. However, this study focuses on neophyte students' perceptions of motivation towards clinical practice.

Purpose of the Study

The aim of the study was to explore the neophyte baccalaureate nursing students' perceptions of motivation regarding clinical practice.

Research Question

What are the perceptions of neophyte baccalaureate nursing students about their motivation towards clinical practice?

Methodology

A qualitative descriptive study design was used to explore the phenomenon of clinical motivation of neophyte nursing students. The study population consisted of second-year baccalaureate nursing (BSN) students enrolled at one of the Private Nursing Colleges in Pakistan. The purposive sampling technique was utilized to recruit participants. Students who had completed the four weeks of clinical experience of the Adult Health Nursing-I course were included in the study. Due to COVID-19, the year one students missed the clinical exposure and therefore were not included in the study. Students who were repeating the course were also excluded. After seeking participants' consent, data were collected and video recorded. In-depth individual interviews were conducted using an open-ended guide. Data were analyzed using the Creswell & Creswell inductive qualitative analysis approach. [11] The data was organized and saved in soft files in the first step. By listening to the recorded interviews, data was transcribed verbatim. In the second step, verification of students' interviews with written descriptions was done by repeatedly reading the transcripts, listening to the recorded interviews, and highlighting the important information and general idea. In the third step, the keywords were noted, and manual coding was done before classifying the subcategories. In the fourth step, the interrelated codes are classified into subcategories and categories. Based on the presentation and characteristics of categories, the theme was generated. In the fifth step, the categories, subcategories, and themes were written narratively. [11] To ensure the rigour of the study, the criteria of Lincoln and Guba's framework of trustworthiness were followed: credibility, dependability, conformability, and transferability. [12, 13] To maintain these criterions, enough time was given to participants to express their perceptions and experiences. The research supervisors and an independent reviewer reviewed the codes and categories developed by the primary researcher. The documentation of coding decisions was done while keeping records of changes. The transcribed data was verified by listening to the audio recordings of the participants. A detailed description of the research process and the participants is provided to the readers to make the meaningful application of the findings to the other context and settings with caution. [12, 13]

Ethical Consideration

Data was collected after getting approval from the Institutional Review Board (IRB # 106-21). Written permission was taken from the Dean of the institution to access the students for the collection of data. Written informed consent was sought from all the participants before conducting the interviews.

Results

Data was collected from nine participants; of these nine, three were male, and six were female. The age of the participants ranged between 20 to 22 years. The subcategories, categories and themes that evolved from the findings are presented in Figure 1 below.

The participants felt that the worthiness of the clinical practice was due to the 'learning opportunities and the possibility of 'integrating theory into practice' for developing their clinical competency. As one participant stated, "*Whatever we study in theory, so it is really important to implement it into real life [patients]. Therefore, clinical practice is quite important*" (p-2). Some participants articulated that clinical practice is an opportunity to interact with patients and implement the theory in real life. They also thought that it could help to care for patients. As one student stated, "*Clinical practice is a good opportunity for*

us to perform whatever we have learned in the skills lab and give patient care properly [competently]" (p-5).

Range of Emotions

Participants shared mixed emotions related to clinical practice, mainly described as 'nervousness and depression' and the 'joy of providing care'. Several participants felt depressed at the beginning of the clinical practice and found it challenging to work; as one participant mentioned, "*When I started clinically, I was very depressed because the clinical is so tough*" (p-1). Students also felt anticipatory anxiety about communicating with the patients and their family attendants. On the contrary, a few students felt the joy of providing care to the patient and receiving appreciation in return. The participants felt good when their patients were comfortable and pain-free because of their care. One participant commented, "*When a patient feels relaxed and comfortable and pain-free because of us, it is motivating, and I feel good*" (p-5). Another participant said, *"I assisted my patient, I gave him back care, and he showered me with lots of prayers, and I was too happy about my job" (p-4).*

Clinical Environment

Most students found that the clinical environment was not conducive to learning. They verbalized that 'restriction on skills' performance', 'lack of respect' and 'communication gap between staff and clinical educators' hindered their learning and motivation. One student responded, "*If the clinical environment is healthy and interactive, it will engage us to work with them [staff]. It will also motivate us to do work" (p-6).* One of the purposes of students' clinical practice is to perform skills and apply the concepts learnt in theory. However, nurses restricted the participants from performing these skills on patients. As one student stated, "*We learn everything in the college, but we cannot perform it in the hospital [patients] because the staff doesn't allow us*" (p-5).

Furthermore, students experienced a lack of respect in the clinical area when the faculty members scolded or provided feedback in front of patients and other healthcare professionals. This behavior encouraged patients' attendants to disrespect students, as one participant stated, "*I was too much insulted in front of them [patient and attendant], so I was too much worried. Faculty should not scold students in front of the patient's attendant. That was not a good experience "(p-4).* A few participants indicated that nurses in Pakistan are not respected. A participant added, "*Here in Pakistan, the nursing profession is quite underestimated. They [the public] do not respect nurses" (p-2).* Most students described that lack of respect in clinical places negatively impacts their motivation, as one expressed that "*this will make the students not to continue their nursing as a career" (p-7*).

Clinical Educators' Roles and Characteristics

Most students expressed being demotivated by clinical educators as they were not facilitated well in the clinical practice. Their main concerns were 'multiple assignments', 'supervision and feedback', longer clinical hours and clinical placement issues. Most of the students expressed that they were given many assignments at the clinical, and they felt difficulty managing tasks. One of the participants mentioned, "*I suggest that [faculty] give fewer assignments; if we have a minimal assignment in one day, then we can easily do it, and we can do brainstorming and make good assignments" (p-8).*

Most of the students expressed the importance of faculty supervision during clinical practice. For example, one participant said, "*I think the teacher should observe. They should be there when we do any skill because they can tell us if we are doing something wrong" (p-4*). The participants expressed the challenge they faced when communicating with their patients. They believed the clinical educator's presence would help them address this challenge. One of the participants said, "*If students face any difficulty while communicating with the patients, the Faculty should communicate with them [patients] so the students can learn from the Faculty (p-7).*

A few participants felt demoralized when clinical educators did not give feedback maintaining privacy. One participant said, "*We should not be insulted in front of the patients or front of the attendants, or the other staff; the faculty should not do that*" (p-4). One more participant added that the impact of maltreatment could be precarious because sometimes they felt like leaving the profession, "*My feeling was not good, I wanted to quit, I wanted to quit this [profession]" (p-3).*

Most students expressed the impact of longer clinical timings on their motivation and learning. They felt that the eight hours of clinical practice per day for neophyte

students were more than required for achieving the clinical objectives. As mentioned by one participant, "*It is very hectic, and it is a very tiring day; whenever you have a clinical, standing from 7 am to 3 pm is difficult" (p-5). One more participant commented, "If the time is more than we need… we start to misuse our duties, we leave early, we will go and stand together, talk and gossip*" (p-9).

Some students found it challenging to care for critical patients when they were assigned to unconscious patients. They were uncomfortable caring for such patients because they were theoretically unprepared. One participant expressed, "*Few patients are in a severe condition, and as a student [neophyte], we cannot see such a critical patient; we were very depressed*" (p-1).

Personal Drive for Clinical Practice

Most participants expressed that regardless of the challenges faced during their clinical practice, the role modelling demonstrated by staff and Faculty, relative being a nurse, and religious and personal beliefs motivated them. For some participants, one motivating factor was the cooperation the staff and Faculty extended to them. As explained by one participant, "*There are some members [nurses], who will allow us to go with them, work with them, that is the most motivating factor for us*" (p-6).

Some participants' motivation was driven by the influence of their relatives in the nursing profession. One participant reported, "*My family has a nursing background, so watching them since my childhood, seeing them wear the white uniform and going for duties motivated me. This has given me the confidence to perform clinical practice" (p-7).*

The participants recognized that clinical practice is essential in nursing education because it helps them apply theory to practice and learn skills. Several factors, such as hospital policies and protocols, uncooperative staff and lack of facilitation by clinical Faculty, demotivated students in clinical practice. However, having a nurse in the family, religious and personal beliefs enhanced their motivation for clinical practice.

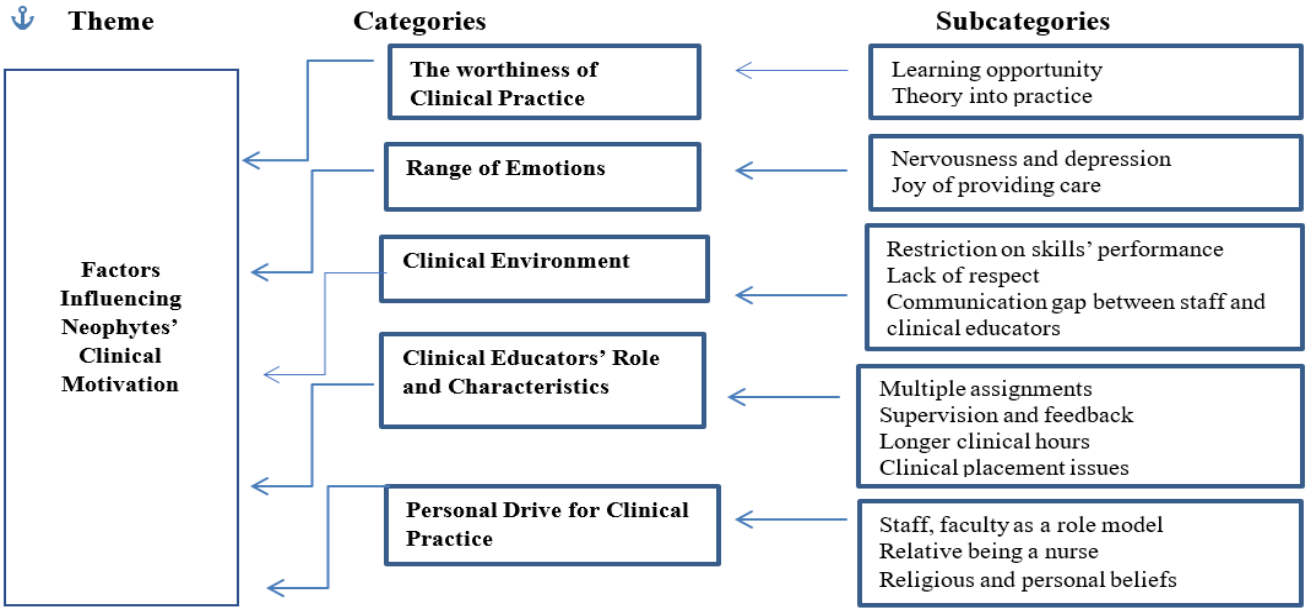

Figure 1: Theme, categories and subcategories emerged from the participants' interview

Discussion

Most of the learning in nursing education occurs in a clinical setting. The participants in the current study also expressed that the clinical experience provides an opportunity to practice skills and apply theory. Amsalu highlights similar findings that clinical practice provides a platform to enhance nursing students' competencies and

allow them to use theoretical concepts.[14] In the current study, the participants felt nervous and anxious at the initiation of the clinical. These results are consistent with the study by Sánchez-Conde, in which nursing students showed anticipatory anxiety in early clinical practice.[15] These findings may help educators to understand the stress associated with the commencement of clinical practice and support students to communicate better and provide pre-orientation of clinical units.[16] Furthermore, utilizing strategies such as peer mentoring and assigning two students to one patient may help neophyte students to support each other during initial clinical rotations.[17]

The study finding about the feeling of distress by participants was attributed to disrespectful behavior, including mistreatment by the Faculty, nurses, and doctors. Jack et al. also reported that healthcare teams do not treat students well; they are ignored and not considered part of the healthcare team.[18] These kinds of behaviors may increase students' psychological issues, such as depression and anxiety, and they may quit the nursing profession. According to Gomathi and Jasmindebora, stress in nursing students may compromise learning and affect patient care.[19]

The current study participants indicated that they were limited to performing learned skills due to the restriction placed by the study setting hospital. It may impact students' learning and create a theory-practice gap.[20] Moreover, these students may harm the patients due to a lack of experience in performing the skills. Thus, there is a need to modify the hospital policy, which restricts students from performing skills. Clinical teachers, nurses and doctors play a significant role in students' motivation. They can teach the students by allowing them to participate in patient care and facilitate their learning. Some of the critical characteristics of an excellent clinical teacher are maintaining good interpersonal relationships with the students, understanding the education needs [5], allocating clinical placement as per the clinical objectives, assigning relevant tasks, managing time effectively, giving students constructive feedback while supervising them in patient care, and most importantly encourage and reinforce them for clinical practice.[21]

In the current study, participants stated that lack of clinical supervision from teachers and staff nurses contributed to their demotivation. When there is a lack of clinical supervision, particularly for neophyte students, serious consequences are possible.[16] As indicated in the current study findings, the students engaged in unethical practices such as filling out the patient's history forms without contacting patients and pretending to be with the patient when Faculty observed. Similar findings were reported in a study conducted in India where the common clinical dishonest behavior demonstrated by undergraduate students was the fake patient details in assignments.[22]

Another finding from the current study was the long clinical hours leading to students' misuse of the clinical time. Clinical educators need to plan clinical schedules and assign tasks to students to ensure effective utilization of clinical timing.[16] Though Pakistan Nursing Council (PNC) has given clear guidelines regarding credit hours for clinical practice, it is the institutions' responsibility to implement the clinical curriculum according to the needs and objectives of the students.[20]

Another important finding was the communication and collaboration gap between the nursing staff and clinical educators. When there is a lack of coordination between education and clinical services, it decreases motivation in students.[6] Additionally, students found that most of the nursing staff were not aware of their clinical objectives, and they expected them to perform beyond their year of study objectives;[22] the learning objectives differ according to the level of studies and the subject's requirements. Therefore, educators must communicate students' objectives to nurses involved in teaching students.

The current study indicated that students' personal and religious beliefs about helping others in need and their family members in nursing motivated their clinical practice. This finding is supported by another Pakistan study in which students were inspired by their relatives in the nursing field and the desire to serve humanity.[10]

Strengths and Limitations of the Study

According to the researchers, this study is one of its kind in Pakistan in exploring neophyte students' perceptions regarding motivation in clinical practice. The two significant limitations of the study were the use of only one private nursing institute for data collection and difficulties noting all the nonverbal gestures of participants, as the interviews were taken on Google Meet due to the COVID-19 pandemic. However, some of the nonverbal

gestures were identified by keeping the video recording on at that time.

Conclusion

Clinical educators, staff nurses, and other health care teams are crucial in motivating neophyte nursing students towards clinical practice. The students can learn better and are well prepared as future nurses if motivation and a conducive clinical environment are provided to them. On the contrary, if students get demotivated from the clinical practice, serious consequences may occur, including compromised safety and quality of patient care. Therefore, nursing institutions and hospital management need to collaborate and modify the policies regarding skills performance and utilizing innovative models of clinical learning to strengthen students' clinical practices. Clinical educators must use a constructive approach when providing feedback to neophyte nursing students.

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ORIGINAL ARTICLE

Psychological side effects of radiation therapy on cancer patients

Fatima Khurshid[1*], Ans Abdul Razzaq[2], Hafsa Khurshid[3]

[1] Medical Doctor, Department of Medicine, Mohi-Ud-Din Islamic Medical College, Mirpur AJK, Pakistan

[2] Dental Surgeon, Department of Dentistry, Islamic International Dental College, Islamabad, Pakistan

[3] Research Scholar, Department of Chemistry, Mirpur University of Science and Technology, Mirpur AJK, Pakistan

Author's Contribution

[1] Conception & design, Data collection.
[2] Data analysis and interpretation, drafting, critical revision and final approval of the article
[3] Writing & technical editing of the manuscript

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Correspondence

Fatima Khurshid
fatimakhurshid61@yahoo.com

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A B S T R A C T

Background: In this study, we investigated the prevalence of anxiety and depression in cancer patients undergoing radiation therapy and identified the factors associated with the multidimensional model, including sociodemographic, clinical, function and well-being, and symptom variables.

Methodology: The research was conducted at the Shifa International Hospital Ltd. in Islamabad's radiation oncology clinic from February 2022 to May 2022. Assessments of side effects and the intensity of typical symptoms experienced by cancer patients receiving radiation therapy have been carried out using the MD Anderson Symptom Inventory (MDASI) questionnaire. Version 20.0 of the Statistical Package for the Social Sciences (SPSS) has been used to analyze the data. They were described using categorical statistics using frequency and percentage.

Results: The majority of participants were women. During the treatment, patients experienced various psychological reactions, such as nausea, Pain, anxiety, depression, fear, fatigue, disturbed sleep, and shortness of breath. Many patients also reported feeling sad, losing enjoyment of life, and having disturbed relationships with people around them. However, the psychological state of patients improved at the end and after the Intervention.

Conclusion: Acute psychological side effects appeared in several patients receiving radiation therapy, such as anxiety, depression, fear, and low self-esteem. Hence, we concluded it has a high incidence. So, radiation therapy patients should receive support and care for their psychological well-being.

Keywords: *Cancer Treatment, Radiation-Induced Psychological side effects, Radiation Reactions, Radiotherapy*

Introduction

Radiation therapy is a frequently used treatment for cancer control or eradication. According to Cancer Facts and Figures 2000, more than a million people are diagnosed with cancer yearly. However, various adverse effects have been linked to localized radiation therapy.[1-4] Radiation therapy frequently causes side effects in cancer patients. Patients with cancer who get radiation therapy often experience psychophysical distress due to common side effects. Severe psychiatric mood disorders can develop from sadness, anxiety, and adjustment difficulties. Following cancer treatment, side effects, particularly fatigue and sleep disturbance, have significantly impacted a patient's quality of life, including job, social, and emotional adjustment.[5-7]

The severity of radiation therapy-related side effects has been strongly linked to psychological distress, as seen by an increase in anxiety, rage, and sadness, in addition to disturbance of daily routines and a lower quality of life.[8, 9] Cancer patients typically indicate that fatigue, rather than the Pain, nausea, and vomiting related to the disease and

treatments, is radiation therapy's most upsetting side effect. All cancer patients should regularly have their levels of fatigue assessed.

This study aims to conduct a literature review and analysis of the psychological effects of radiation treatment on cancer patients to learn more about how patients perceive RT and associated processes.[11] This study aimed to assess how radiation therapy affected the psychological components of cancer patients' quality of life. To investigate the impact of the Intervention on the severity of side effects resulting from radiation therapy for various malignancies, a randomized clinical trial including patients was conducted. The informative Intervention for the patients will be based on factual information about what to anticipate during their therapy.[1]

In this study, we looked at the frequency of anxiety and depression in cancer patients receiving radiation therapy and will determine the variables connected to the multidimensional model, including sociodemographic, clinical, function and well-being, and symptom variables. In this study, we investigated the prevalence of anxiety and depression in cancer patients undergoing radiation therapy and will identify the factors associated with the multidimensional model, including sociodemographic, clinical, function and well-being, and symptom variables.

Methodology

This study has been carried out on clinically and histopathological diagnosed cancer patients undergoing radiotherapy at the Radiation Oncology clinic of Shifa International Hospital Islamabad. The sample included a statistically substantial convenience of 100 diagnosed cancer patients who were undergoing radiation therapy in the period between Feb 2022 to May 2022 with the following inclusion criteria; Biopsy proven malignancies, diagnosed cancer patients undergoing RT, Patients receiving RT at the Radiation Oncology clinic of Shifa International Hospital Islamabad and Ability to communicate effectively with the study personnel. The findings were supported by a cross-sectional survey study that explored functioning, emotional distress, and symptoms in cancer patients undergoing radiation therapy. The survey was conducted using a standardized questionnaire, the MDASI core items, to evaluate the intensity of symptoms that patients experienced and the disruption of daily activities.

The MD Anderson Symptom Inventory (MDASI) is a patient-reported outcome (PRO) assessment for several symptoms in clinical and research contexts. Use the MDASI to assess the severity of the symptoms that cancer patients report and the disruption to everyday functioning that these symptoms create. [12] The 13 symptom items that make up the core MDASI were those found to occur most frequently and severely in patients with a range of malignancies and treatment modalities. The MDASI is a brief assessment of the impact and severity of cancer-related symptoms. It has 15 main symptoms in all.

Each symptom is graded on an 11-point scale (0–10) to reflect its severity and presence over the past 24 hours (0–10 = "as bad as you can imagine"). Six symptoms that interfere with how a patient's life has been functioning during the past 24 hours are also included. The interference items are scored on a scale of 0 to 10, with 10 denoting complete interference. [11] In the past three months, radiation patients with cancer have been the subject of analysis. The study only included patients who met the requirements for inclusion, and survey data were used for analysis. Data has been analyzed using Statistical Package for the Social Sciences (SPSS), version 20.0. The frequency and percentage of categorical data were used to describe them.

This research study was ethically approved by the Institute Review Board (IRB) & Ethics Committee of Shifa International Hospital Islamabad (Ref: IRB # 251-21). All the patients were selected from the outpatient department. All the patients signed informed consent papers and voluntarily participated in the study. We assured the confidentiality of the participants.

Results

Radiation therapy's physical and psychological side effects can significantly affect a patient's general activity, walking, working, enjoyment of life, and mood. Patients may experience anxiety, depression, fear, fatigue, nausea, skin irritation, and changes in body image or self-esteem, leading to decreased social functioning, decreased ability to work, and decreased overall quality of life. The sample consisted of 100 cancer patients who were on radiotherapy. Regarding clinical data, all the patients

included in this study were clinically and histopathological diagnosed cancer patients. All the patients completed radiation treatment. Most participants comprised women; 62% and 38% were men.

In this study, all the patients developed some sort of psychological reaction, such as nausea, in 58% (1.23±1.774) patients. The Pain was exhibited by 57% (1.62±2.399) patients, fatigue was seen in 81% (0.66±1.799) patients, 59% (1.07±1.689) of the population complained of disturbed sleep, 81% (0.51±1.219) patients were distressed during the treatment, 36% (2.61±2.348) of the population experienced shortness of breath during the procedure. The 29% (3.01±2.672) patients experienced dry mouth, 36% (2.15±2.376) of the population experienced feelings of sadness, 39% (1.89±2.132) patients complained of loss of enjoyment of life, 62% (0.75±1.5) people felt disturbed relationship with people around them, 66% (0.89±1.614) people complained of uneasy walking, 65% (0.88±1.701) population complained of work being affected.

Generally, activity of daily life was found to be disturbed in 66% (1±1.896) of the population. 42% (2.28± 2.466) people experienced mood swings, 64% (1.31±2.078) people felt drowsy after the procedure, 16% (3.79±2.626) population experienced numbness and tingling sensation, 81% (0.82±2.002) population had vomiting & 42% (2.11±2.399) people experienced loss of appetite during the procedure. The overall psychological state of patients was improved at the end and after the Intervention.

Table 1: MDASI Score items used to assess the psychological impact of radiation therapy on cancer patients

MDASI Symptom Items	Symptom severity	Mean	Standard Deviation
Pain	57%	1.62	2.399
Nausea	58%	1.23	1.774
Numbness/Tingling	16%	3.79	2.626
Disturbed Sleep	59%	1.07	1.689
Distressed/Upset	30%	2.61	2.348
Sadness	81%	0.51	1.219
Dry Mouth	29%	3.01	2.672
Shortness of Breath	36%	2.15	2.376
Lack of Appetite	42%	2.11	2.399
Drowsiness	64%	1.31	2.078
Walking	66%	0.89	1.614
Vomiting	81%	0.82	2.002
Difficult Remembering	82%	0.69	1.74
Fatigue	81%	0.66	1.799
General Activity	66%	1	1.896
Walking	66%	0.89	1.614
Working	65%	0.88	1.701
Enjoyment of life	39%	1.89	2.132
Relations with people	62%	0.75	1.5
Mood	42%	2.28	2.466

Discussion

Radiation therapy is used in curative, palliative, and preventative treatment strategies, depending on the kind of cancer and the desired goals of the procedure. It can be administered via external beam, internal insertion, or systemic delivery. Radiation therapy affects a cell's DNA, which prevents it from proliferating. Malignant cells generally cannot repair the radiation-induced damage, but healthy, noncancerous cells typically recover from radiation therapy. Radiation exposure to noncancerous cells is minimized through careful treatment planning, minimizing side effects. The use of radiosensitizers and radioprotectants is a part of this.[10-14] A cancer diagnosis significantly impacts emotional well-being. It's common to experience these kinds of life-altering emotions after a diagnosis. These feelings are typical and healthy; straightforward people should deal with them.

An individual may experience exhaustion from starting cancer treatment, such as radiation therapy, which can result in emotional discomfort and anxiety. Radiation therapy has an impact on both your thoughts and feelings in addition to your physical health.[15, 16] The sort of radiation side effects the patient experience varies on the dose and schedule recommended. Most adverse effects go away within a few months of treatment being finished. Some adverse effects could continue even after treatment since it takes time for healthy cells to recover from radiation. Specific adverse effects may limit your capacity to do certain tasks. Some patients with radiation therapy can attend work or participate in leisure activities while undergoing treatment. Some people work less well and require more sleep than usual.[17]

Compared to the Pain, nausea, and vomiting brought on by the malignancy and therapies, the most upset side effect of radiation therapy is frequently found by cancer patients to be weariness.[10] Vomiting and nausea are frequent and occasionally dangerous adverse effects of

cancer treatment. Cancer therapies such as chemotherapy and radiation can make patients feel queasy and sick. These symptoms might range from minor to major. If the patient is undergoing radiation therapy applied to substantial areas of the body, especially the GI system, liver, or brain, the likelihood of experiencing nausea-related symptoms increases. Radiation therapy also damages the cells that line the intestines, making these regions more susceptible. In contrast to diarrhoea, which can happen at any time of the day, nausea and vomiting are frequently experienced shortly after the treatment. Patients probably feel better when they don't receive radiation therapy.[15] It's crucial to manage and reduce nausea and vomiting. These issues may impact daily activities, mental and physical health, and even treatment if they are not addressed. A crucial component of cancer care and therapy is relieving side symptoms, commonly known as palliative or supportive care.[16]

Even if the patients obtain the recommended amount of rest and sleep, they may still feel physically, emotionally, and mentally exhausted. Patients often feel worn out. In patients undergoing multiple types of treatments, such as radiation therapy and chemotherapy, the level of weariness may rise.[15] The most frequently reported symptom of cancer and its treatment is exhaustion or fatigue. It's normal to have extreme fatigue while receiving radiation therapy. It can be due to the physical demands of the treatment, as well as the emotional stress of dealing with cancer. Fatigue can also be a side effect of cancer itself. Many things, like stress, discomfort, or anaemia, can contribute to or make one feel more exhausted. Fatigue can be minor to severe, depending on each person's general health. Cancer-related fatigue is commonly characterized by exhaustion after resting and a lack of energy for daily duties.[16]

Sometimes receiving radiation to the breast might result in radiation pneumonitis, an inflammation of the lungs. Radiation pneumonitis is the medical term for lung inflammation caused by radiation therapy to the chest (or, less frequently, the breast). It may occur three to six months after getting radiation therapy. If you also have emphysema, which results in the progressive destruction of lung tissue, your chances of developing this condition increase. One of the primary symptoms of radiation pneumonitis is breathlessness, which usually worsens with effort, weakness, coughing, chest pain, etc.[17] Radiation treatment to the head, face, or neck may cause a dry mouth. The salivary glands may take up to six months or longer to start producing saliva after radiation therapy is done. Dry mouth generally improves within the first year after radiation therapy. But many people continue to have chronic dry mouth to some extent. It is prevalent if radiation therapy is administered to the salivary glands, but several ways exist to decrease or prevent this. ASCO suggests using radiation therapy techniques, including intensity-modulated radiation therapy (IMRT), that reduce radiation exposure to the salivary glands.[15]

Radiotherapy-induced peripheral neuropathy is a persistent disability that may be worrying because it advances and is frequently irreversible. It typically develops several years after treatment. With longer-term cancer survival rates improving, its rarity is rising. We still don't fully comprehend the pathophysiological mechanisms. However, cytokines released from cancer cells during RT can damage adjacent noncancerous cells. This inflammatory reaction can result in nerve damage in the form of fibrosis, atrophy, ischemia, or ulceration of vessels and nerves.[18] In addition to reducing saliva production in the morning, radiation therapy also affects appetite by generating symptoms of xerostomia, taste sensitivity, analgesic use, and oral mucositis. Depending on the dose and schedule of radiation therapy, different precautions should be taken to prevent a decrease in appetite brought on by side effects. These findings give healthcare professionals crucial knowledge they need to comprehend, encourage proper nutritional intake, and improve the quality of life for cancer patients undergoing radiation treatment.[18]

Conclusion

For cancer patients, radiation therapy is a frequent form of treatment. While it can effectively destroy cancer cells, it can also have psychological side effects on patients. These side effects can vary in severity and affect patients during and after treatment. Radiation therapy's physical and psychological side effects can significantly affect a patient's general activity, walking, working, enjoyment of life, and mood. Patients may experience fatigue, weakness, and changes in body image or self-esteem, making it difficult to perform daily activities like walking or

working. These physical side effects can also lead to decreased enjoyment of life and may contribute to feelings of depression and anxiety. Additionally, anxiety and depression can further impact a patient's mood and quality of life. The treatment can be a stressful and frightening experience, and patients may worry about the potential side effects and long-term effects of radiation exposure.

After radiation therapy, patients may continue to experience psychological side effects. They may worry about the cancer returning or the long-term effects of radiation exposure. They may also experience changes in body image or self-esteem, especially if the treatment causes scarring or other physical changes. Therefore, patients need to receive support and care for their psychological well-being during and after radiation therapy, including counselling, support groups, or other forms of treatment, and to talk openly about their feelings and concerns with their healthcare providers and loved ones. Healthcare professionals can assist patients in maintaining their quality of life and enhance their general mood by addressing treatment's physical and psychological components.

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ORIGINAL ARTICLE

Apprehension among medical students while dealing with patients: A cross-sectional study in a private sector medical college and teaching hospital

Saad Amir Zaman[1*], Shahroz Zahid[2], Umer Ijaz[3], Amna Khan[4], Ramsha Abbas[5]

[1-5] Medical Graduate of Shifa College of Medicine, Shifa International Hospitals Ltd., Islamabad, Pakistan

Author's Contribution

[1] Planning, data collection, analysis, manuscript writing
[2] Planning, literature review, data collection, manuscript review
[3] Planning, methodology, data collection, manuscript review
[4-5] Planning, questionnaire, data collection, manuscript review

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Correspondence

Saad Amir Zaman
saadamir96@gmail.com

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A B S T R A C T

Introduction: Beginning to deal with patients can be a testing experience for medical students. Many schools have endeavored to understand students' perceptions and acclimatize them to the stresses of clinical work with success.

Objective: This study aimed to identify undergraduate students' apprehensions when dealing with patients, explore the underlying causes of these apprehensions, examine gender differences in apprehension levels, and investigate any effect of patient encounters on career choices.

Methodology: This cross-sectional study was conducted on third, fourth and fifth-year medical students of Shifa College of Medicine, selected by simple random sampling. Data was collected using a self-administered questionnaire. Statistical analysis was done using Statistical Package for the Social Sciences (SPSS).

Results: Results showed that 22.5% of the students felt significant apprehension when dealing with contagious patients, 11.2% with psychiatric patients, and 13.0% with terminal patients. Male students exhibited more apprehension than female students when interacting with female patients of similar age (p=0.0001) and middle age (p=0.020). Greater apprehension was felt in the Emergency Room (mean 2.66) as compared to in-patient (2.07) and community clinic (1.82). The highest level of apprehension was in the presence of a consultant (51.5% answered either 4 or 5). 128 students (75.7%) believed they would be less apprehensive if they saw more patients.

Conclusion: Specific apprehensions among medical students were identified when interacting with different types of patients. Gender differences, clinical settings, and the presence of consultants influenced apprehension levels. Increasing patient exposure was seen as one solution to reduce apprehension.

Keywords: *Apprehension, Medical students, Patients, Interaction*

Introduction

Exposure to the clinical setting as an undergraduate medical student is a vital part of medical education, bringing the aspiring doctor in contact with patients, the ultimate object of their studies. In this transition from books to patients, various methodologies are employed to deliver knowledge, including actual history taking, physical examination, morning reports, and "classroom" activities (lectures, workshops and simulations). With this "human element" in their lives, students now face unique burdens in addition to their ongoing theoretical learning. Burdens such as the fear of making mistakes, coping with responsibility and facing with inexactness of medicine were highlighted in a study.[1] Different students cope with them in different ways, and with their learning and mental health intimately tied to how well they manage to adjust to this change, it is essential to identify any significant apprehensions regarding dealing with patients.

This point is better elaborated in research, which showed that high social anxiety scores among medical undergraduates correlated with negative communication skills and attitudes.[2] Exploring such perceptions may uncover specific modifiable sources of tension, possibly helping improve student-patient interaction, which will benefit student learning and confidence and the community, which currently needs skillful and critically empathizing "human" doctors.

Methodology

Study Design

It was a cross-sectional study. Our sample population were students of Shifa College of Medicine, located in Islamabad, who were in their 3rd, 4th or 5th year of studies and had completed at least one clinical rotation. 1st and 2nd-year students, those who had not completed at least one clinical rotation and those who did not consent were excluded.

Sample Size

Using Open EPI (proportion mode), a sample size of 169 was calculated. Participants were selected via simple random sampling.

Questionnaire

A self-administered questionnaire was employed, which used most close-ended questions with some open-ended questions regarding personal bio-data and a single open-ended question that called for an explanation if applicable. The close-ended questions involved the Likert Scale that was arranged into five levels, from no apprehension to intense apprehension, and the option of having never interacted with the kind of patient asked in that question. The questionnaire was distributed both online and in printed form.

Statistical Tests and Variables

Various questions were asked, so sections arranged them according to bio-data, participants' confidence in their basic sciences knowledge, the effect of type of patient on apprehension, apprehension in different clinical encounters, and the effects of dealing with patients on various aspects of participants' attitudes. The variables in this study are nominal, ordinal and dichotomous. The following listed are the variables:

1. Gender
2. Age
3. Year of study
4. Apprehension in different clinical settings
5. Effects of patient interaction on various aspects of student life, including career choice

A combination of the chi-square test, t-test, and one-way ANOVA were used as appropriate. All data were entered into the IBM Statistical Package for the Social Sciences (SPSS) Software and analyzed accordingly.

Ethical considerations

Institutional Review Board (IRB) approval was obtained before conducting this study. Consent was taken at the beginning of the questionnaire, and all information provided by the participants was kept confidential.

Results

A total of 169 MBBS students of 3rd, 4th and 5th year completed the questionnaire. Basic profile of the study participants is listed in Table 1.

Table 1: Basic profile of participants

Gender	Male	N=75
	Female	N=94
Median age (range)	22 years (range = 7; 20 to 27)	
Number of students in each year	3rd year	N=55
	4th year	N=55
	5th year	N=59
Percentage of students residing in a hostel	26.0% (N=44)	
Percentage of students with a doctor in their close family	52.7% (N=89)	

Participant's feelings in the hospital environment:

Participants were asked about feeling overwhelmed, anxious, fearful, nervous or sorrowful in the hospital. 36 students (21.3%) felt overwhelmed, while the most common feeling was nervousness (68), followed by anxiety (44), sorrow (39) and fear (14). 64.5% of participants believed their knowledge of the basic sciences was

adequate for their clerkship activities (109 out of 169 answered "yes").

Effect of type of patient on apprehension:

The respondents were asked to score apprehension on a scale of 0 to 5 while dealing with the following types of patients:

- Those with a contagious disease
- Those with a psychiatric illness
- The terminally ill

Their scores were grouped into three categories:

1. Not applicable, or NA (if they chose 0: Never interacted, or 3: Unsure)
2. Insignificant apprehension (if they chose 1: No apprehension or 2: Some apprehension)
3. Significant apprehension (if they chose 4: Strong apprehension or 5: Very strong apprehension)

The results are summarized in Figure 1.

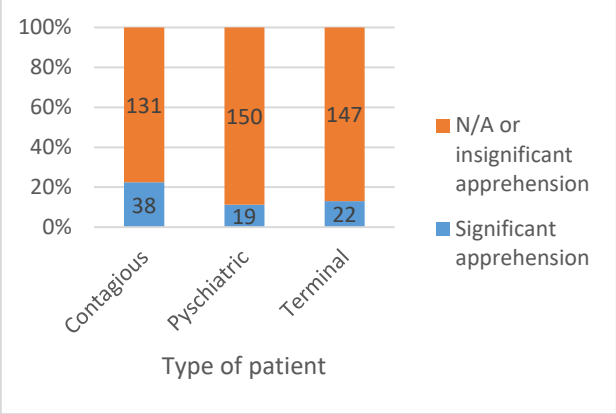

Figure 1: Percentage of participants with Significant Apprehension for each type of patient.

Apprehension in different clinical encounters:

They were asked to score their apprehension on a scale of 1 to 5 while dealing with male and female patients separately for three different age groups (similar age, young, middle-aged/elderly). To test the association between the gender of the patient and apprehension, a Chi-square test was applied. It was significant for $p<0.05$ when applied to the "similar age, female patient" category ($p = 0.0001$), as well as the "very young, female" category ($p = 0.0001$). It was insignificant for the "similar age, male patient" category ($p = 0.257$). It was also not significant for all the other age groups.

A t-test was performed to compare the mean apprehension score of male students with female students in each age category. It was significant only in two categories, with male students having a higher mean apprehension score in each: the "similar age, female patient" group (mean score for males = 2.28 vs females = 1.39; $p = 0.0001$) and the "middle-aged/elderly female patient" group (mean for males = 2.04 vs females = 1.67; $p = 0.020$). It implies that male students are more apprehensive while dealing with patients of the opposite gender, while female students are unaffected by the gender of the patient. The mean scores are illustrated in Table 2.

Table 2: Comparison of mean apprehension scores for male and female students for different ages and genders of patients; p values in bold are significant.

Age and gender of the patient	Score Male students Mean (SD)	Score Female students Mean (SD)	P-value
Similar age, male	1.59 (0.946)	1.87 (1.050)	0.068
Similar age, female	2.28 (1.097)	1.39 (0.858)	<0.0001
Very young male	1.83 (1.107)	1.55 (0.838)	0.069
Very young female	2.11 (1.158)	1.48 (0.839)	<0.0001
Middle-aged/elderly male	1.81 (0.926)	2.01 (1.000)	0.190
Middle-aged/elderly female	2.04 (1.071)	1.67 (0.977)	0.020

They were asked to score their apprehension while working in the following three settings:

- Community clinic (Falahi OPD)
- Shifa International Hospital (SIH)/In-patient
- Emergency (ER)

The one-way ANOVA test compared the participants' mean scores in these settings. The test was significant ($p < 0.00001$), with ER having the highest mean score (2.66), followed by SIH/In-patient (2.07) and then Falahi OPD (1.82). Apprehension was scored in each of the following six clerkships:

- Surgery

- Gynecology/Obstetrics
- Medicine
- Ear, nose and throat (ENT)
- Ophthalmology
- Paediatrics

To compare the mean scores of 3rd, 4th and 5th-year students in each clerkship, the one-way ANOVA test was performed, which was significant, for $p<0.05$, for all clerkships except surgery as in Table 3.

Table 3: Mean score and post hoc analysis for each year and clerkships

Clerkship	Mean score for 3rd year (standard deviation)	Mean score for 4th year (standard deviation)	Mean score for 5th year (standard deviation)	p-value (One-way ANOVA)	Multiple comparisons (Post-**hoc Tukey's test)**
Surgery	2.53 (1.168)	2.13 (1.139)	2.10 (1.322)	0.120	Not applicable
Gynecology/Obstetrics	2.53 (1.289)	2.84 (1.330)	2.12 (1.205)	0.012	4th year higher than 5th year (p=0.010)
Medicine	2.16 (1.151)	2.00 (1.089)	1.51 (0.728)	0.002	3rd higher than 5th (p=0.002) and 4th higher than 5th year (p=0.018)
ENT	1.87 (1.055)	1.76 (0.981)	1.41 (0.746)	0.022	3rd year higher than 5th year (p=0.024)
Ophthalmology	1.76 (1.138)	1.62 (0.733)	1.32 (0.730)	0.026	3rd year higher than 5th year (p=0.048)
Paediatrics	1.96 (1.018)	2.16 (1.198)	1.58 (0.855)	0.009	4th year higher than 5th year (p=0.010)

Further, a Chi-square test was performed to determine any association between the gender of the student and apprehension score in each clerkship. It was found to be significant for two clerkships: Gynecology/Obstetrics ($p = 0.0001$) and Pediatrics ($p = 0.002$). The independent samples t-test was also significant, with males having a higher mean apprehension score in each group: $p = 0.0001$ for Gynecology/Obstetrics (mean for males = 3.07 vs females = 2.02) and $p = 0.001$ for Pediatrics (males = 2.24 vs females = 1.62). The apprehension score in the presence of a consultant had the highest mode of all the scenarios (mode = 4). 87 students answered either 4 or 5, the highest percentage (51.5%) for all the questions in this setting; there was no significant difference between male and female students based on the t-test ($p = 0.154$).

Effects of dealing with patients on various aspects of participants' attitudes:

Participants were asked to score a positive or negative impact of dealing with patients on the following aspects:

- Their learning
- Their empathy for patients
- Their self-esteem
- Their confidence

The overall response was positive. For effect on their learning, 85.3% (144) of participants chose either "4: Some positive effect" or "5: Strongly positive effect". For empathy, self-esteem and confidence, the percentages are 82.2% (139), 67.5% (114) and 78.1% (132), respectively. When asked whether patient exposure will make them better doctors, 84.1% agreed (142). They were also asked about the effect of patient exposure on their career choice if they had decided before 3rd year. 64 participants had not made

a career choice. For the remaining 105 students, Figure 2 illustrates the results.

They were asked if seeing more patients or fewer patients would decrease their apprehension; 75.7% (128) of students believed seeing more patients would make them less apprehensive, 6.5% (11) believed seeing fewer patients would reduce apprehension and 17.8% (30) believed several patients would not affect their apprehension. When asked if they thought patient exposure before 3rd year would decrease apprehension, 56.2% agreed (95). Finally, 58.6% (99) believed workshops would help reduce their apprehension.

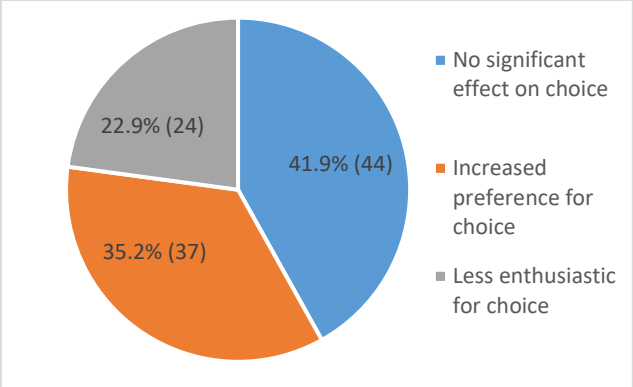

Figure 2: Number and percentage of each response.

Discussion

The most significant statistical finding so far is that male students are more apprehensive than female students while dealing with similar-aged and middle-aged/elderly patients of the opposite gender. It is similar to the results of a study performed in the UK, which showed that the genders of the patient and student interacted powerfully and that female students were more patient-centered than male students. [3] Another study on medical students in the US found that female students have more positive attitudes towards communication skills training than male students.[4] It may provide context to the results of our study that perhaps male students are more apprehensive due to a perceived disregard for the significance of communication skills.

This interaction of doctor-patient gender also affects patients, as a study at a hospital in Toronto, Canada, showed that having a male doctor was the most commonly perceived hindrance to effective communication.[5] This implies that gender issues should be targeted, preferably starting in student life, to benefit health professionals and patients. For all the different clerkships, except for surgery, students of other years had significantly different apprehension levels.

It includes gynecology/obstetrics, in which male students showed greater apprehension than female students. It appears to correlate with the results of another study which showed that the only factor that significantly affected the perception of gynecology/obstetrics was gender.[6] Perhaps apprehension is one factor influencing preference for gynecology/obstetrics as a career. Apprehension in the ER was significantly higher compared to clinic and in-patient settings. Whether this affects students' preference for emergency medicine as a career should be explored because various studies show that students who pursue emergency medicine have different influences and attitudes, including apprehension.[7, 8]

The majority of our students believed that the effect of interacting with patients was positive. They also believed that more exposure to patients in the pre-clinical years (1st and 2nd years) would decrease apprehension. Therefore, we may recommend that students be involved more in patient care as early as the first year, as advised by a study on medical students' perceptions of their learning regarding interacting with patients in Brazil.[9] It is unlikely to adversely affect the quality of healthcare services.[10] Our study was limited by the intrinsic limitations of the Likert scale and the inclusion of only a single college.

Conclusion

Specific apprehensions among medical students were identified when interacting with different types of patients. Gender differences, clinical settings, and the presence of consultants influenced apprehension levels. Increasing patient exposure was seen as one solution to reduce apprehension. These findings may guide institutions in designing effective interventions and support systems to address and alleviate the apprehensions faced by students during clinical training.

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ORIGINAL ARTICLE

A spectrum of severity and prevalence of malignant hyperthermia in anesthetized patients with inhalational anesthetic

Abrar Khan[1], Muhammad Imran[2], Amjad Hayat Khan[3], Yaseen Hussain[4], Fazlullah khan[5*]

[1] Anesthesia Technologist, Department of Anesthesia, Bashir Institute of Health Sciences, Islamabad, Pakistan

[2] Anesthesia Technologist, Department of Anesthesia, Bashir Institute of Health Sciences, Islamabad, Pakistan

[3] Assistant Professor, Department of Anesthesia, Bashir Institute of Health Sciences, Islamabad, Pakistan

[4] Lecturer, Department of Pharmacy, Bashir Institute of Health Sciences, Islamabad, Pakistan

[5] Assistant Professor, Faculty of Pharmacy, Capital University of Science and Technology, Islamabad, Pakistan

Author's Contribution

[1-2] Write-up and Data Collection

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[4] Editing and data analysis

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Correspondence

Fazlullah khan

fazlullahdr@gmail.com

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A B S T R A C T

Introduction: Malignant hyperthermia (MH) or hyperpyrexia is a pharmacogenetic syndrome of skeletal muscles caused by volatile anesthetics such as halothane and depolarized muscle relaxant suxamethonium. The prevalence of MH in Islamabad has not been explored.

Methodology: This was a retrospective study on the severity and prevalence of MH in anesthetized patients with inhalational anesthetics Clinical data from the previous years, i.e. from June 2020 to June 2021, from eight tertiary care hospitals in Islamabad was collected.

Results: Out of 40,900 patients discharged from these hospitals under general anesthesia, only 07 patients were diagnosed with MH due to anesthesia. MH is associated with gender; in our study, more incidence was observed in males than females. Of the seven patients with MH, four (57.14%) were males, and three (42.86%) were females. The prevalence rate of MH was 0.018% due to anesthesia in surgical patients which is approximately 1 per 5842 cases.

Conclusion: This research study concluded that the prevalence rate of MH in Islamabad is 0.018%. The prevalence rate for males is slightly higher than for females. According to this statement, the total number of male patients who got MH was four, and females were three out of 40900 surgical cases under general anesthesia in a specific year of duration. The prevalence of MH due to anesthesia in surgical patients treated in Islamabad hospitals is approximately 1 per 5842 cases. MH risk in males is significantly higher than in females.

Keywords: *Anesthesia, Inhalation anesthetics, Malignant hyperthermia*

Introduction

Anesthesia is the state of controlled change or temporary loss of sensation for medical purposes. The patient becomes unconscious, either entirely or partially. It might incorporate a few or all of the absence of pain (help from or counteraction of agony), loss of motion (muscle unwinding), amnesia (loss of memory), and obviousness.[1] Anesthesia aims to achieve the point required for surgical procedures with at least risk for the patient. Anesthesia is generally used for surgical procedures.[2]

General anesthesia is a therapeutically actuated trance-like state with loss of defensive reflexes because of the organization of at least one available sedative specialist. It is completed to permit operations that would somehow or another be grievously excruciating for the

patient or where the idea of the basic technique blocks the patient from being conscious.[3]

Anesthesia is administered by various routes, e.g., inhalational, injection (Intramuscular, Intravenous, or subcutaneous), oral, and rectal. General anesthetics are induced either inhalational or intravenous. Intravenous is faster than inhalation, taking about 10-20 seconds to cause total unconscious. Some anesthetic induction agents are propofol, ketamine, thiopental, etomidate, and methohexital.[4] Regional anesthesia should not be applied to surgical procedures needing muscle relaxants and analgesia. Such technique also should not be used for general anesthesia involving abdomen, thoracic, shoulder, neuro, cardiac, head and neck surgery.

However, anesthesia risks are generally associated, e.g., obstructive sleep apnea, where the patient stops breathing while sleeping; seizures; existing cardiac, renal, or lung diseases; hypertension; alcoholism; history of reactions to anesthesia and MH. The MH is the most lethal risk factor of general anesthesia.[6] It is a genetic disorder of skeletal muscle that is caused by certain drugs used for anesthesia (e.g., isoflurane, sevoflurane, halothane, Desflurane, Enflurane) and depolarizing muscle relaxants (e.g., suxamethonium).[6, 7] MH is manifested by hyper digestion caused by calcium entry from the sarcoplasm reticulum, high oxygen consumption, and unexplained CO_2 expansion that doesn't diminish with expanding minute ventilation, tachycardia, hyperthermia, and respiratory and metabolic acidosis.

Different indications of MH might cause intravascular coagulation, heart arrhythmias, hyperkalemia, hypophosphatemia, hypocalcemia, and marbled skin.[6, 7] Other symptoms include increased end-tidal carbon dioxide, skeletal muscle rigidity, muscle spasm, tachycardia and sweating.[8, 9] The incidence of MH during general anesthesia is 1:10,000 up to 1: 250,000. While in the case of females, the incidence of MH is less common than in young male patients within the age limit of under 30. In contrast, MH is less common in ages above 30. [10] This research aims to identify the range of severity and prevalence of MH in patients anesthetized with an inhalational anesthetic agent. According to a survey conducted in 2008 in Japan, a total of 187,097 cases were performed under general anesthesia in Japan in one month. The survey included a total number of cases served 1,238,171 under general anesthesia in 18 months. The result showed that the prevalence of MH in Japan's population (13.7 per million) in 2006-2008 was similar to the previous year (16.6 per million).[11] According to the North American report of 2007 – 2012, the cases of MH fatality rate have increased by up to 10%, and morbidity and mortality of MH when the administration of dantrolene is delayed. The administration of succinylcholine without volatile anesthetics resulted in 24 MH events. One patient died, while fourteen suffered severe complications.[12-14] MH is an intriguing issue.

MH in inpatient settings has emerged as an exciting issue, and it has been reported from managerial information and records that MH's defenselessness is a compelling issue. Revealed pervasiveness of MH analysis in examinations utilizing emergency clinic release records from administrative information goes from 0.18 per 100,000 (95% certainty span (CI), 0.12-0.25) in wandering a medical procedure place patient to 0.96 (95% CI, 0.75-1.41) in careful inpatients.[6, 15]

The lowest recurrence of MH emergencies and the expense of loading dantrolene have led to worry about the money-saving advantage of the suggestion of the MH Association of the United States (MHAUS) that dantrolene be made promptly accessible (for organizations inside 10 min) in working room regions, particularly in offices with low usage of general anesthesia and setting off specialists like maternity units.[16] MH Association of the United States is a patient security and support association, and its suggestions are utilized by certifying offices, like the Joint Commission, to evaluate readiness for an MH occasion during review visits. Notwithstanding, no review has explicitly inspected the commonness of MH powerlessness in obstetric patients.[14]

Methodology

This research is a retrospective study in which we aimed to determine the severity and prevalence of MH in anesthetized patients with inhalational anesthetics The study population for this research included all surgical procedures under general anesthesia visiting eight tertiary care hospitals of Rawalpindi and Islamabad. Data was collected after approval from the Ethics and Research Committee of Bashir Institute of Health Sciences Islamabad and respective private hospitals from where

data was collected. A–validated questionnaire was used to collect data, and all the surgical procedures under general anesthesia were observed/recorded by visiting eight tertiary care hospitals in Rawalpindi and Islamabad. The study was conducted from September to December 2021. The sample size for this research was 40900.

The nonprobability convenience sampling method was used for data collection. Data were analyzed through SPSS software version 22. All surgical procedures under general anesthesia were included in this research study. Patients under ten years and those who used suxamethonium were excluded.

Results

Demographic analysis:

We calculated the percentage and frequency of total suspected MH cases in which the frequency of males was 4 while that of females was 3. The rate of male suspected cases was 57.14%, and female was 42.86%, shown in Table 1.

Table 1: Frequency of Genders

Gender	Frequency	Percentage
Male	4	57.14
Female	3	42.86
Total	7	100.0

Frequency of age:

Table 2 shows the age and frequency of patients. We have 7 patients (4 males and 3 females) of different ages. The age of 7 MH suspected patient is 12, 23, 24, 28, 33, 43 and 55. Among them, the percentage of all seven patients was 100 and 14.3 individually for every patient.

Descriptive Analysis:

Table 3 shows the total number of cases from June 2020 to June 2021 in eight main hospitals at Islamabad and Rawalpindi with a minimum of 1520, maximum of 9360 and mean of 5112.5.

Table 2: Frequency of age

Age	Frequency	Percentage
12	1	14.3
23	1	14.3
24	1	14.3
28	1	14.3
33	1	14.3
43	1	14.3
55	1	14.3
Total	7	100

Table 3: Total Number of cases

	N	Minimum	Maximum	Mean
Cases	40900	1520	9360	5112.5

The following formula calculated the prevalence of MH:

Prevalence = No. of cases /total number of cases X 100
= 7/40900 X 100
=0.018%

The prevalence rate of MH:

Table 4 shows the prevalence rate of MH in total cases. The total number of surgical patients under GA was 40900, with 7 MH suspected cases. So the prevalence rate was 0.018%.

Table 4: Prevalence rate of MH

Total surgical cases under GA	Total MH cases	Prevalence rate
40900	7	0.018%

Association of MH with other variables:

Table 5 shows an association of MH with gender, in which the male ratio was higher than the female. There were 4 males, and 3 female patients were suspected.

Table 5: Association of MH with gender

	Gender		
	Male	Female	Total
MH	4	3	7

Association of MH with age:

Table 6 MH is associated with age; in which we have seven different ages of patients. The age seven MH suspected patients are 12, 23, 24, 28, 33, 43 and 55.

Table 6: Association of MH with age

Age	Age							Total
	12	23	24	28	33	43	55	
MH	1	1	1	1	1	1	1	7

The severity of MH:

This chart (Figure 1) shows the severity of MH in total suspected patients out of total surgical cases. The chart shows the temperature, $PaCO_2$, muscle tightness, respiratory, and heart rate. The temperature was more significant than 98.6F; the $PaCO_2$ was greater than 45 mmHg. Muscle tightness during surgery, the respiratory rate was higher than 25, and the heart rate was more than 100b/m.

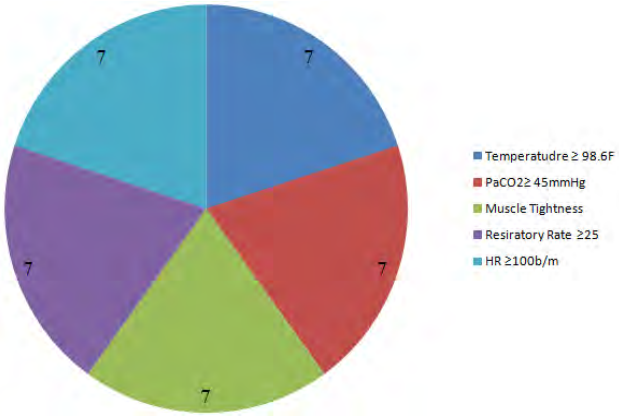

Figure 1: Pie chart showing the average percentage of temperature, $PaCO_2$, muscle tightness, respiratory rate, and heart rate.

Discussion

This study revealed that the prevalence of MH is scarce in Islamabad, Pakistan. There were 40900 total surgical cases operated under general anesthesia from June 2020 to June 2021 in eight tertiary care hospitals of Islamabad with a minimum of 1520, maximum of 9360, and mean of 5112.5. This research study showed that only seven diagnosed cases of MH were reported out of 40900 surgical cases under general anesthesia. The prevalence rate of MH was 0.018%. According to Brady et al., 12,749,125 patients were discharged from New York state hospitals from 200 to 2006; however, MH was diagnosed in only 73 patients. The percentage of male-diagnosed cases was 57.14%, and that of females was 42.86%, showing that the frequency of MH cases in males versus females is 4:3.[6]

In another study conducted in Japan in 2008, 1,238,171 patients underwent general anesthesia, out of which 344,224 (27.8%) cases were in emergency hospitals and 893,947 (72.2%) in local area hospitals. In this patient population, MH was diagnosed in only 17 patients; the prevalence rate of MH was 0.00138.[15]

Our research study demonstrated that the frequency of males was 4 and females was 3 in total suspected MH cases. Our analysis also revealed that the percentage of male suspected cases was 57.14%, and females were 42.86%. In conformity with the current study's findings, a work done by Masahiko Sumitani stated that male patients were more susceptible to MH than females. According to a recent report by American and Japanese that the prevalence of MH is most common in patients under 30 years of age and less common in patients above 30 years of age.[16]

This research study showed the spectrum of severity, which revealed that the temperature was higher than 98.6F, the $PaCO_2$ was more than 45 mmHg, there was muscle tightness during surgery, the respiratory rate was higher than 25, and the heart rate was also more than 100b/m. These findings were also investigated in a research study by Brady, J.E in Japan, the first MH models set by the Japanese anesthetist that extensively utilized two variables expanded body temperature increased than 40°C increasing respiratory rate than 25. An increase in

heart rate of 100b/m and other symptoms of MH, muscle tightness, and metabolic acidosis.[6]

Conclusion

This research study concluded that the prevalence rate of MH at Islamabad and Rawalpindi was 0.018%. The prevalence rate of males is slightly higher than females. The total number of male patients who got MH were four, and female were three out of 40900 surgical cases under general anesthesia in one year. All patients suffering from MH demonstrated severe symptoms of increased temperature higher than 98.6 °F, the PaCo2 is more than 45 mmHg, muscle tightness during surgery, elevation in a respiratory rate higher than 25, and increased heart rate than 100b/m.

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ORIGINAL ARTICLE

Melody of sleep by sun: Association between serum vitamin D levels and sleep quality in ESRD patients

Zoha Fatima[1*], Ujala Abdul Rashid[2], Umara Nasim[3], Hafiza Amina Muattar[4]

[1] House Officer, Department of Medicine, Rawalpindi Medical University, Rawalpindi, Pakistan

[2] Post Graduate Trainee, Department of Medicine, Rawalpindi Medical University, Rawalpindi, Pakistan

[3] Medical Officer, Department of Medicine, Bilal Hospital, Rawalpindi, Pakistan

[4] Post Graduate Trainee, Department of Community Medicine, Akhter Saeed Hospital, Lahore, Pakistan

Author's Contribution

[1] *Article writing*

[2] *Data analysis and article writing*

[3] *Data Collection*

[4] *Literature review*

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Correspondence

Zoha Fatima

xohafatimah@gmail.com

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A B S T R A C T

Background: Hemodialysis (HD) is a commonly employed treatment modality for chronic kidney disease (CKD) patients. Along with its other effects on the body, hemodialysis is also closely related to the sleep-wake cycle. It has both sleep-improving and deteriorating results. Sleep regulation is tightly coupled to vitamin D; hence, its deficiency might impact the duration and quality of sleep. This study intends to evaluate the association between sleep quality and serum vitamin D levels in HD patients.

Objective: To assess the quality of sleep in patients with ESRD on routine HD and determine the association of vitamin D deficiency with sleep quality.

Methodology: This cross-sectional analytical study was conducted on the patients presenting to the dialyzing centre of the Department of Nephrology, Holy Family Hospital, Rawalpindi, Pakistan, for twice-weekly routine hemodialysis, from May 2022 to June 2022. The chi-square or Pearson test evaluated correlations between the variables. Odds ratios (OR) were obtained using linear regression with 95% CIs (confidence intervals).

Results: In this study, the quality of sleep in End Stage Renal Disease (ESRD) patients on twice-weekly hemodialysis (HD) was assessed using the PSQI score. PSQI scores were associated with serum vitamin D levels in these patients. A significantly strong positive correlation existed between serum levels of 25-OH D and sleep quality ($r = -0.468$, $p = 0.001$).

Conclusion: More than half of the patients undergoing routine hemodialysis could not sleep well at night. Among other related factors, vitamin D deficiency was an independent risk factor for poor sleep quality. Further studies are needed to determine the impact of vitamin D supplementation on improving sleep quality to strengthen the association between vitamin D levels and sleep disorders.

Keywords: *ESRD, Hemodialysis, PSQI score, Vitamin D*

Introduction

Sleep is a form of self-healing, and it occupies 20-40% of the day of an average human being. However, patients suffering from CKD commonly face the problem of poor sleep quality.[1] The health-related quality of life (HRQOL) is an effective tool for assessing patients' comprehensive perception of mental, physical, and emotional health, and it is accepted as a health outcome. Poor sleep quality directly correlates with the decline in HRQOL, leading to poor quality of life.[2] As hemodialysis is the primary treatment modality in ESRD, studying the effects of hemodialysis on the quality of sleep has recently caught the attention of healthcare providers. About 50-80% of patients undergoing hemodialysis experience sleep quality deterioration.[3]

Hemodialysis is closely related to the sleep-wake cycle of the patient. It not only confers the benefits of sleep-inducing effects by limiting mobility, accelerating interleukin-1 production, increasing body temperature, and altering the brain's osmotic imbalance, leading to reduced consciousness.[4] On the other hand, it also comes with many disadvantages, such as sleep apnea syndrome, restless leg syndrome, sleep disturbances, and excessive anxiety during the day, thus reducing sleep quality and duration. After a while, these sleep disturbances may lead to 'day-night reversal', that is, insomnia at night and sleepiness during the day, depressed mood, headache, and reduced daytime functionality.[4]

Poor sleep represents an independent predictor of mortality in HD patients.[5] Furthermore, and it can cause the development of cardiovascular diseases and sleep apnea, which can serve as a primary cause of death in patients with renal disease. A sleep span of fewer than 5 hours is associated with a rapid decline in renal function compared to sleeping 7–8 hours in healthy people.[6] Sleep deprivation also harms the body's immune responses.[7] Therefore, early diagnosis and timely action are necessary to improve these patients' sleep quality.

According to studies, 86.8% of CKD patients experience sub-optimal Vitamin D levels, as CKD is a risk factor for Vitamin D deficiency.[8] Multiple factors may contribute to vitamin D deficiency in patients with CKD, such as limited exposure to sunlight, impaired epidermal synthesis of vitamin D, impaired hepatic conversion of cholecalciferol to calcidiol, decreased intake of Vitamin D-rich foods, and inadequate absorption of vitamin D from the GI tract.[9] The sleep-wake cycle regulation is closely linked to vitamin D; hence, its deficiency harms sleep quality.

Vitamin D, directly and indirectly, affects circadian rhythm, as 25-OH D receptors (VDRs) have been found in the brain regions involved in sleep.[10] Recently, it has been suggested that vitamin D has an essential role in serotonin and melatonin regulation that, in turn, modulate the regulation of mood and sleep.[11, 12] Through this study, we aim to examine the possible association between serum vitamin D levels and sleep disturbance in HD patients. Multiple studies have shown that the prevalence of low sleep quality has become a common problem in ESRD patients.

Thus, patients' sleep quality needs to be evaluated periodically. So, the modifiable factors, including hypovitaminosis D can be duly addressed, and proper supplementation is undertaken to improve the quality of life of CKD patients.

Methodology

This cross-sectional analytical study was conducted on 97 patients presenting to the dialyzing centre of the Department of Nephrology, Holy Family Hospital, Rawalpindi, Pakistan, for twice-weekly routine hemodialysis. The study was conducted from May 2022 to June 2022. Inclusion criteria were all ESRD patients aged 18-75 who have been on twice-weekly HD for at least the last three months and have given informed consent to participate in the study. The pediatric group of age less than 13 years and patients having any pre-defined independent risk factor that can adversely affect the quality of sleep, like anaemia (Hb < 10), diabetic nephropathy, or any active inflammatory state, was not included in the study. Similarly, patients with dementia, mental retardation, major depressive disorder, severe pulmonary diseases, acute heart failure, and a history of hospitalization within the last six months were also excluded from the study. After considering the inclusion and exclusion criteria, the study was conducted on 82 patients, out of which two patients lost follow-up due to changes in the dialysis centre and death, respectively. So, the final analysis was done on 80 patients.

Serum levels of 25 (OH) D were evaluated in patients before dialysis. Venous blood samples were withdrawn and sent to a well-known authentic laboratory affiliated with the department under strict protocols of care. The assay was performed via Chemiluminescent Microparticle Immunoassay (CMIA), and results were recorded as the standard unit of ng/ml. The patients were divided into three groups based on KDOQI guidelines: Sufficiency: >30 ng/ml, insufficiency: 16-30 ng/mL, mild deficiency: 5-15 ng/mL, and severe deficiency: <5 ng/mL.[13]

The Pittsburgh sleep quality index (PSQI) standard questionnaire was obtained from https://aurora.edu/documents/wellness/assessment.pdf. Previously, it has been used in and validated by multiple studies, and the specificity and sensitivity of this questionnaire have been well-defined.[14, 15] The

questionnaire was clearly explained to the patients and the data was collected through detailed interviews. The questionnaire consists of seven components. A global PSQI score between 0 to 21 was obtained by adding the score of individual components. The patients were divided into two groups based on their PSQI scores: a score of ≥ 5 suggests poor sleep quality and a score of < 5 is a marker of good sleep quality.[16]

Plan for Statistical Analysis: Data obtained were entered and analyzed via SPSS version 25. The patient's demographic and clinical characteristics were expressed as the mean ± SD (standard deviation). The prevalence of poor sleep quality and vitamin D deficiency in the sample population was calculated. Variables with normal distribution were analyzed by t-test. The chi-square or Pearson test evaluated correlations between the variables. Odds ratios (OR) were obtained using linear regression with 95% CIs (confidence intervals). $p \leq 0.05$ was considered significant.

Results

Our study assessed the sleep quality in 80 CKD patients on twice-weekly HD using the PSQI score obtained from a unit global questionnaire. PSQI scores were associated with serum vitamin D levels in these patients, as in Figure 1.

The mean age of participants was 42.9 ± 15.07 years; 48.3% (n=35) were women, and 51.7% (n= 45) patients were men. Various types of vascular access were used for HD procedures depending on the individual preferences and feasibility; 67.5% of patients had an arteriovenous fistula (AV fistula) (n = 54), 10.0 % had a permanent catheter (n = 8) and the rest of 22.5 % had double-lumen catheter (DLC) (n =18).

Furthermore, the initial indication for starting hemodialysis was assessed among patients. It was calculated that 71.25 % (n = 57) of patients had hypertensive nephropathy, 16.2 % (n = 13) of patients had AKI progressing to CKD; 8.75 % (n = 7) patients had chronic interstitial nephritis, and three patients (3.7 %) suffered from autosomal dominant polycystic kidney disease (ADPKD) that led to the initiation of hemodialysis.

The average PSQI score among the study population was 8.61 ± 5.66. 63.7 % (n = 51) of the population shows PSQI score ≥ 5, representing significant sleep disturbance. The people with poor sleep quality have a mean PSQI score of 12. The mean serum levels of 25 (OH) D (ng/ml), Ca, Mg, and P were 19.09 ± 15.59, 9.28 ± 0.98, 3.048 ± 0.82, and 3.963 ± 1,44, respectively. A significantly strong positive correlation existed between serum levels of 25-OH D and sleep quality ($r = -0.468$, $p = 0.001$). However, observations showed no significant correlation between age and patients' sleep disorders ($p = 0.093$) and no correlation between sleep quality and gender ($p = 0.290$). Similarly, no significant association was found between the quality of sleep and serum PTH ($p = 0.417$), serum Ca ($p = 0.654$), serum Mg ($p = 0.095$), and serum phosphate ($p = 0.750$), as in Table 1 and 2.

Table 1: Demographic and clinical characteristics between patients with good and poor quality sleep

Characteristics	Patients with Good Sleep Quality	Patients with Poor Sleep Quality	*p-value*
Number (%age)	29 (36.3%)	51 (63.7%)	
Age (years)	39.45 ± 11.48	45.00 ± 16.53	0.093
Gender: Men Women	 16 (20 %) 13 (16.25 %)	 29 (36.25 %) 22 (27.5 %)	0.290
Vitamin D (ng/ml)	29.21 ± 21.86	13.33 ± 4.80	0.001
Serum Calcium	9.48 ± 0.94	9.17 ± 0.99	0.654
Serum Magnesium	3.01 ± 0.47	3.06 ± 0.96	0.095
Serum Phosphate	3.84 ± 1.31	4.03 ± 1.52	0.750
PTH	555.66 ± 550	331.10 ± 506	0.417
Duration of hemodialysis (years)	11.25	12.67	
Mode of access for HD			
AV fistula	31 (38.75 %)	23 (28.75 %)	0.334
Perma Cath	03 (3.7 %)	05 (6.2 %)	
DLC	11 (13.7 %)	07 (8.7 %)	
Initial Indication for Hemodialysis			
Hypertensive Nephropathy	30 (37.5 %)	27 (33.7 %)	0.087
AKI Progressing to CKD	08 (10 %)	05 (6.2 %)	
Chronic interstitial nephritis	04 (5.0 %)	03 (3.7 %)	
ADPKD	03 (3.7 %)	00 (0 %)	

Table 1: Correlation between the studied variables in patients with poor quality of sleep (PSQI Scores >5)

Variables		Age	Vitamin D	Calcium	Magnesium	Phosphate	PQSI score	PTH
Age	*r*	1	-.090	-.144	-.040	.078	.170	-.222
	p-value		.427	.201	.721	.490	.133	.048
Vitamin D	*r*	-.090	1	.232	.046	-.049	-.468	.047
	p-value	.427		.039	.686	.666	.001	.676
Calcium	*r*	-.144	.232	1	.038	-.054	-.197	-.133
	p- value	.201	.039		.741	.634	.080	.239
Magnesium	*r*	-.040	.046	.038	1	.024	-.137	.045
	p-value	.721	.686	.741		.835	.227	.692
Phosphate	*r*	.078	-.049	-.054	.024	1	.041	.270
	p-value	.490	.666	.634	.835		.720	.016
PQSI score	*r*	.170	-.468	-.197	-.137	.041	1	-.318
	p-value	.133	.001	.080	.227	.720		.004
PTH	*r*	-.222	.047	-.133	.045	.270	-.318	1
	p-value	.048	.676	.239	.692	.016	.004	

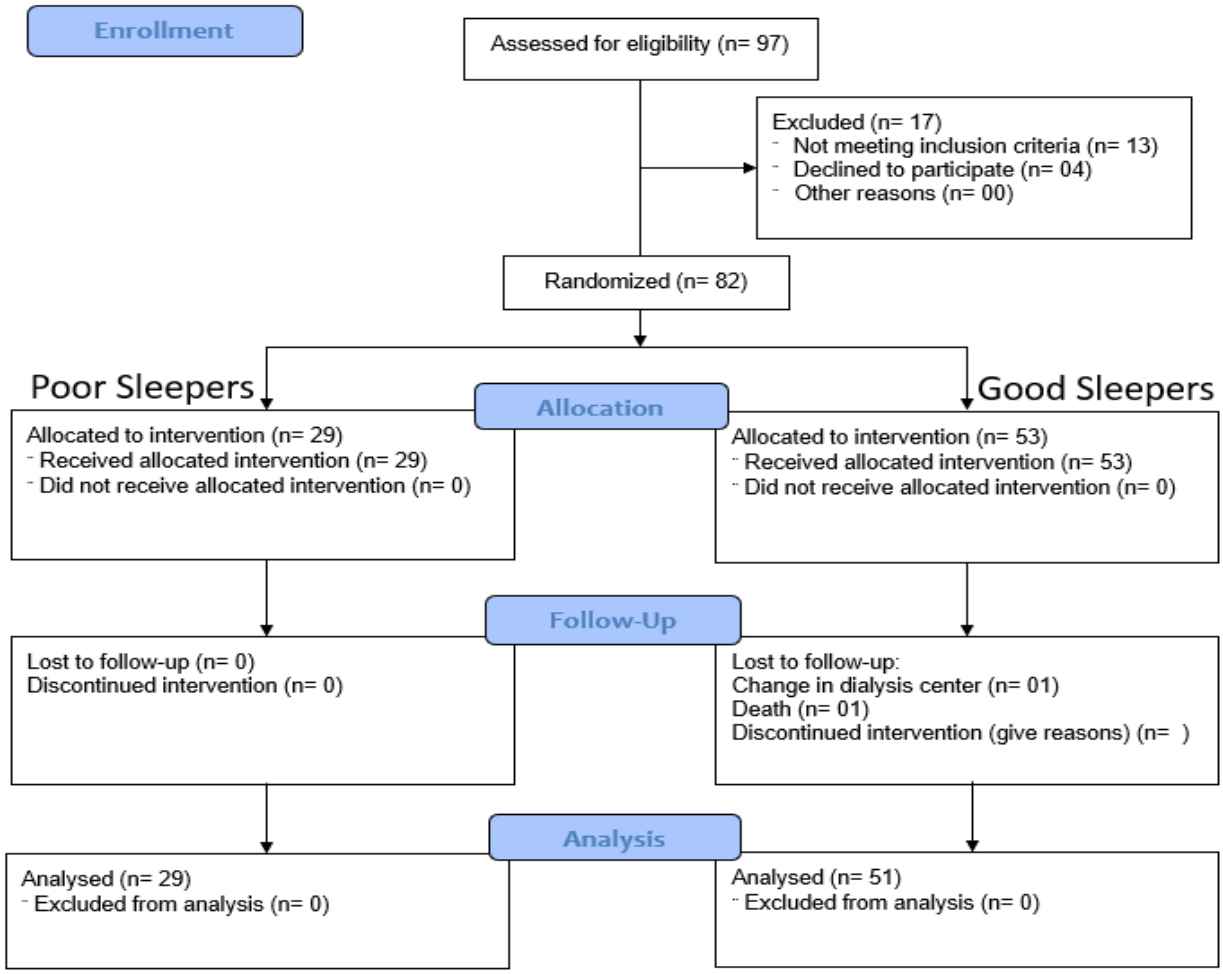

Figure 1: The CONSORT 2010 flow diagram for hemodialysis patients

Discussion

Our study demonstrated that a significant percentage of patients suffering from CKD were experiencing poor sleep quality. Similar large-scale studies have been conducted in China and Korea, concluding that poor sleep might be an independent risk factor for CKD.[17-19] Poor sleep quality in CKD patients results from interlinked processes. The many factors involved make it challenging to designate a single causative agent as the sole cause of disturbed sleep patterns. These can be ESRD-specific factors like anaemia, obstructive sleep apnea, restless leg syndrome, and other comorbidities, metabolic acidosis, uremia, hypertension, diabetic nephropathy, and nephrogenic pulmonary oedema; psychological disorders including depression or anxiety; lifestyle factors (coffee/nicotine use, sleep hygiene) and treatment-related factors, which encompass dialysis shift timing, dialysis disequilibrium syndrome, side effects of medications as well as personal habits like daytime napping and disruptions in circadian rhythm.[20, 21] On the contrary to that, there are few other studies with limited sample sizes (n < 500) that have reported that individuals with poor sleep quality had better renal function as compared to others.[22]

These overlapping phenomena highlight the difficulty in assessing sleep disorders for clinical or research purposes and suggest that the issue should be dealt with comprehensively by applying a multi-layered approach. That's why the association between sleep quality and all these factors has been subjected to research repeatedly.

One of the modifiable factors brushed aside was hypovitaminosis D. In the past, few studies showed a negative correlation between serum vitamin D levels and sleep quality in CKD patients.[23] Furthermore, other studies suggested a strong association between vitamin D and quality of sleep in patients suffering from other diseases like systemic lupus erythematosus and elderly adults. [24, 25] Encouraged by past reports, we conducted this relatively smaller-scale study to find the association between 25-OH D levels and sleep quality in patients with CKD, which has yielded similar results.

Patients with CKD usually have vitamin D deficiency, considering that the cutoff limit for vitamin D in CKD is higher than in healthy adults, i.e., 30 ng/dl. Vitamin D plays diverse roles in the human body bone turnover, control of the inflammatory response, and cellular differentiation. Therefore its deficiency is closely related to disease progression and mortality. [26, 27]

It is also seen that in severe kidney hyperparathyroidism, PTH plays a pivotal role in causing sleep disorders, and parathyroidectomy could markedly alleviate these symptoms in about half of the patients undergoing HD.[28, 29] Even after adjusting confounding factors such as serum Ca, P, and PTH levels, the result remains the same, with a negative correlation between vitamin D levels and sleep quality.[23] Vitamin D supplementation has proven to be relatively safe and effective in patients undergoing HD [30, 31,] but it is also one of the most economical and accessible means of improving the overall patient quality of life index. Quite a few RCTs have previously shown that by increasing the serum level of vitamin D, the scores obtained from the PSQI questionnaire in these patients decreased, and as a result, the quality of sleep was improved. One such trial was conducted in 2008, which proved that daily oral supplementation of 25-OH D in doses as low as 10-30 mg/d entirely resolved vitamin D deficiency in HD patients while maintaining a high safety profile. However, this matter is still debatable as vitamin D supplementation might not show notable improvement in sleep quality, as observed in similar studies. [32]

Considering these contradictory results, we suggest a better interventional study involving multiple centres, as the present study showed some technical setbacks. As a cross-sectional study with a small sample size, not only could it establish a causal relationship between observed variables, it didn't rule out a possible bidirectional relationship either. The information was collected from a single dialyzing centre via self-reporting, and there might be recall bias, miscalculation, and lack of diversity.

The high incidence and underdiagnosis of nephrogenic pulmonary oedema, sleep apnea, restless leg syndrome, and insomnia in CKD patients necessitate well-designed experimental studies with large sample sizes and ethnic diversities. Upcoming research should target the complex interrelationships between sleep and kidney disease and, as a result, propose innovative treatments for sleep disorders that can take the multifaceted physiological and psychosocial challenges these patients go through. We

also suggest routine assessment of the sleep quality of patients to improve the overall quality of life, repeated measurements of vitamin D levels, and oral supplementation at regular intervals to take appropriate steps towards improving these effortlessly changeable yet commonly overlooked factors.

Conclusion

This study concluded that more than half of the patients undergoing routine hemodialysis were unable to get sound sleep at night. Among other related factors, vitamin D deficiency was an independent risk factor for poor sleep quality. Further studies can be conducted to determine the impact of vitamin D supplementation on improving sleep quality to strengthen the association between vitamin D levels and sleep disorders.

Recommendations

- Patients suffering from CKD commonly face the problem of poor sleep quality. Out of these, about 50-80% of hemodialysis patients experience deterioration in sleep quality.
- Poor sleep quality directly correlates with the decline in the Health-Related Quality of Life Index (HRQOL), leading to poor quality of life. It also represents an independent predictor of mortality in HD patients.
- Multiple factors contribute to vitamin D deficiency in patients with CKD, so much so that 86.8% of CKD patients experience sub-optimal Vitamin D levels.
- Vitamin D, directly and indirectly, affects circadian rhythm as 25-OH D receptors (VDRs) have been found in the brain regions involved in sleep. So, it has been found through multiple studies that vitamin D levels directly impact the patient's sleep quality.

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Effect of seasonal changes on frequency of eclampsia in patients presenting to Ayub Teaching Hospital

Aneesa Fawad[1], Bushra Zardad[2], Humaira Jadoon[3*], Ayesha Ismail[4]

[1] Professor, Gynae B Unit, Ayub Teaching Hospital, Abbottabad, Pakistan

[2] Registrar, Gynae B Unit, Ayub Teaching Hospital, Abbottabad, Pakistan

[3] Assistant Professor, Gynae B Unit, Ayub Teaching Hospital, Abbottabad, Pakistan

[4] Postgraduate trainee, Gynae B Unit, Ayub Teaching Hospital, Abbottabad, Pakistan

Author's Contribution

[1] Conception and design

[2] Data analysis and interpretation

[3] Literature review

[4] Data collection, data analysis and proof reading

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Correspondence

Humaira Jadoon

drmairan@gmail.com

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A B S T R A C T

Introduction: Eclampsia is an acute obstetrical emergency carrying high maternal and perinatal morbidity and mortality. High blood pressure during pregnancy after 20 weeks of gestation is associated with proteinuria and generalized tonic-clonic convulsions. The purpose of the study is to observe seasonal variation in the presentation of eclampsia in a tertiary-level hospital.

Methods: This is two years study conducted in the Gynae A unit, Ayub teaching hospital, Abbottabad, from January 2021 to December 2022. The study included all the patients admitted to the unit with eclampsia. It included antenatal patients and patients who developed eclampsia in labour or perpurium. Patients with a history of fits due to epilepsy or any other neurological disease were excluded from the study. Statistical analysis of data was done using SPSS version 16.

Results: Total number of admissions during two years period was 7166. The total number of patients admitted with eclampsia during this period was 88 (1.22 %). The majority of patients were in the age group between 21 to 35 years (78.3%). There were 52 primigravidas out of 88(59.1%). There were 46 multigravidas (40.9%). During the fall and winter seasons, 46 patients with eclampsia were admitted (52.1%). 25 admissions were in the spring months (28.4%), and 17 admissions (19.3%) during the summer months. All patients belonged to poor socioeconomic groups. All were unbooked. 78 patients out of 88(88.6 %) belonged to areas more than 25 kilometres away from a medical facility. The season was cross-tabulated with different variables, and no statistical significance was found.

Conclusion: Eclampsia is a severe obstetrical emergency usually involving young primigravidas with poor socioeconomic status and no antenatal care. Primary prevention is regular antenatal care. Early referral and time management will reduce maternal and perinatal morbidity and mortality. The incidence of eclampsia is more in the fall and winter seasons.

Keywords: *Eclampsia, Seasonal variation, Maternal and perinatal morbidity*

Introduction

Eclampsia is an acute obstetrical emergency. This complication is specific to pregnancy. It is characterized by high blood pressure, proteinuria and generalized tonic-clonic convulsions. Pregnancy-induced hypertension is high blood pressure that develops denovo in pregnancy after 20 weeks of gestation. It is defined as BP 140 /90 mmHg or more on two occasions 4 hours apart. Proteinuria is a urinary protein loss of more than 300 mg in 24 hours. When combined with pregnancy-induced hypertension, it is called preeclampsiac toxaemia. Preeclampsia is a multisystem disorder of pregnancy. Eclampsia is a serious

complication of preeclampsia, with the patients presenting with generalized tonic-clonic convulsions.[1]

Preeclampsia and eclampsia are disease theories, and the exact cause is unknown. The pathogenesis lies in the ischaemic placenta, which releases vasoactive factors into general circulation. These factors give rise to endothelial-mediated end-organ damage and produce clinical manifestations of the disorder.[2]

Complications of eclampsia include placental abruption, acute renal failure, cerebrovascular accidents, cardiovascular complications, cardiac arrest, respiratory arrest, DIC, HELLP syndrome, and maternal and perinatal mortality. Well-recognized risk factors for preeclampsia and eclampsia include chronic hypertension, chronic renal disease, Diabetes, obesity BMI >35 kg/m2, nulliparity, past and family history of preeclampsia, SLE, antiphospholipid syndrome, and seasonal changes involving changes in temperature, humidity and barometric pressure.[3]

There is an association between preeclampsia and eclampsia with changing seasons and weather. Different studies have shown different results, but most studies have demonstrated the occurrence of the disorder in winter.[4]

Methodology

This study was conducted in the Gynaes B unit at Ayub Teaching Hospital Abbottabad, a tertiary-level hospital. It was a two years study starting from January 2021 to December 2022. Inclusion criteria were all those antenatal patients with eclampsia and patients who developed eclampsia during labour and perpeurium. Patients with a history of fits due to epilepsy or any other neurological disorders were excluded from the study. The diagnosis was based on typical history and clinical examination. After admission, patients were managed according to the set protocol of the unit for eclampsia. Data were collected retrospectively from hospital records on a previously designed proforma.

Statistical analysis:

Data was entered in SPSS version 16 and analyzed. The chi-square test was applied, and a P value <0.05 was considered significant. Means and medians were calculated for numerical variables, and percentages and frequencies were calculated for categoric variables.

RESULTS

Over two years, 88 patients with eclampsia were in 7166 obstetric admissions (1.22%). Most patients were aged 21 to 25 years (29.5%), the mean age was 26.13 years and its median was 23 years. There were 52 primigravidas (59.1%) and 36 multigravidas (40.9%). In 63 patients (71.6 %), the gestation period at the presentation time was 29 to 36 weeks. 26 patients (29.5%) were admitted in the winter months.

The 20 patients (22.7%) were received in autumn. Only 17 patients (19.3%) were received in the summer months. 78 patients (88.6%) belonged to areas more than 25 kilometres away from the hospital. 60 patients (68.1%) needed operative delivery. Crosstabulation of the season was done with different variables, and the P value was found to be statistically non-significant.

Table 1: Age-wise data

Years	Frequency	Percentage
20 or less than 20	18	20.5
21 to 25	26	29.5
26 to 30	20	22.7
31 to 35	23	26.1
35 to 40	1	1.1
Total	88	100.0

Crosstabulation of the season with age showed the P value to be 0.186 (statistically not significant).

Table 2: Parity-wise data

Years	Frequency	Percentage
Primipara	52	59.1
parity 2 and 3	26	29.5
para 4 and above 0	20	11.4
Total	88	100.0

Crosstabulation of the season with parity showed the P value to be 0.287 (statistically not significant)

Table 3: Gestation-related data

Years	Frequency	Percentage
Less than 28 weeks	8	9.1
29 to 36 weeks	63	71.6
More than 36 weeks	17	19.3
Total	88	100.0

Crosstabulation of the season with gestational age showed a P value to be 0.107 (statistically not significant).

Table 4: Season-wise data

Weathers	Frequency	Percentage
Winter (Dec, Jan, Feb)	26	29.5
Spring (March, April, May)	25	28.4
Summer (June, July, Aug)	17	19.3
Autumn (Sep, Oct, Nov)	20	22.7
Total	88	100.0

Table 5: Distance-related data

Distance	Frequency	Percentage
Less than 25 km	10	11.4
More than 25 km	78	88.6
Total	88	100.0

Crosstabulation of the season with hospital distance showed the P value to be 0.517 (statistically not significant).

Table 6: Delivery states

Mode of Delivery	Frequency	Percentage
Vaginal delivery	28	31.8
Caesarean section	26	29.5
Hysterotomy	34	38.6
Total	88	100.0

Table 7: Neonatal outcomes

Neonatal Outcome	Frequency	Percentage
Alive	43	48.9
Stillbirth	36	40.9
Neonatal death	9	10.2
Total	88	100.0

Table 8: Maternal outcome

Maternal Outcome	Frequency	Percentage
Discharged home alive and healthy	79	89.8
Maternal mortality	9	10.2
Total	88	100.0

Discussion

Most of our patients were young and in the age group (21-35 years). Most of them (52%) were primigravidas. One year study conducted in Liaqat University Hospital Jamshoro Hydrabad by Fouzia Sheikh and her team analyzed 188 patients of eclampsia among 4979 obstetrical admissions. The frequency of eclampsia was common in young primigravidas (78%) with a lack of antenatal care. [4] Kirsten Duckit, in a study, described the risk factors for preeclampsia and eclampsia and mentioned these conditions to be more common in teenage pregnancies and primigravidas.[5]

Most patients belonged to the poor socioeconomic group and were brought to the hospital from far-flung mountainous areas where the approach to the hospital is difficult.78 patients out of 88(88.6%) belonged to areas more than 25 kilometres away from the facility. There is a lack of awareness to avail antenatal services and their importance for the health of the mother and baby during pregnancy. Poverty and illiteracy aggravate the situation. Presentation is usually delayed. Initially, patients are taken to local doctors or hospitals and referred to tertiary-level hospitals with intensive care facilities. Such delays worsen the patient and baby's condition and adversely affect management's outcome. Surraya Halimi and her colleagues also mentioned these risk factors in a study conducted at Saidu Teaching Hospital Swat.[6] The population's weather conditions and social circumstances are the same in Swat as in the Hazara division.

Preeclampsia and eclampsia are still the leading cause of maternal and fetal morbidity and mortality in our country after haemorrhage. The etiology of this condition is multifactorial, and the incidence is increasing with time despite improvements in the provision of antenatal services. Environmental factors, dietary factors, lifestyle measures, weather and climate influence disease frequency.

We received 88 patients with eclampsia over the period of 2 years. There were 7166 obstetrical admissions (1.22%). The 26 patients were admitted in the winter season and 20 in the fall, so 46 patients with eclampsia were received in cold weather. 25 patients out of 88 (25%) were admitted in the spring months, and 17/88 (19.3 %) of patients were received in the summer months. A study conducted by Fauzia Fahim and her colleagues in Lady Reading Hospital Peshawar also analyzed the season's effect on eclampsia frequency. A 4 years study from 2005 to 2008 analyzed 810 patients of eclampsia in 20, 132 births. The frequency of eclampsia was highest in winter (4.925%) in December; it declined during spring and was lowest in summer (3.29%).[7]

Within our country, studies from different provinces yield different results regarding the effects of seasons on preeclampsia and eclampsia. Interesting results are shown in a study conducted at Jinnah postgraduate medical centre Karachi by Raana Jamelle. Data were collected from 4 large government teaching hospitals in four provinces of Pakistan. All four provinces have different climate conditions with wide variations in temperature and humidity. In Sindh and Punjab, the summer is harsh and prolonged, and the frequency is more in the hot season, while in KPK and Balochistan, where winter is more severe, the frequency is more in cold weather.[8]

Pregnancy-induced hypertension, preeclampsia and eclampsia are progressive manifestations of the same pathophysiologic condition. The disorder is more common in developing countries with poverty, illiteracy and lack of antenatal care. These are the prime factors to be addressed to reduce the incidence of this disorder. Early diagnosis and timely management will always make the difference.[9]

A study conducted by Utpal Gosh and his team in eastern India studied the effects of season and weather conditions on the incidence of eclampsia. That part of India has a high incidence of eclampsia. The study included the patients' data over the period of 36 months from 2010 to 2012 and analyzed that the incidence of eclampsia was highest in winters(39.21%), followed by monsoon and post-monsoon season (35.87%)and lowest in hot weather (24.09%).[10]

A study was conducted in the tropical climate of Mumbai, India, by Vidya Subramaniam—the aim was to assess the correlation between preeclampsia and eclampsia between monsoon and dry weather. Monsoon was cold and humid, with low barometric pressure than the rest of the year. Data was collected from a large maternity centre in Mumbai over 36 months (1993 to 1996). There were 29562 deliveries. Among them, there were 34 patients with eclampsia (11%). The incidence was highest in monsoon (2%). Low temperature and high humidity were identified as triggering factors for eclampsia.[11]

In the review of global literature, it was evident that different seasons and weather conditions affect disease incidence and progression. A study from Iran by Fatemeh Janani and Farah Naz Changaee showed their results after analyzing 8000 pregnant women admitted to hospital in labour. The overall prevalence of preeclampsia was 3.8 %. The highest prevalence rate of 4.5% was observed in summer, and the lowest (2.7%) in winter. Prevalence was highest in July. The incidence of pregnancy-induced hypertension and preeclampsia was more elevated in mothers having delivery in the summer months.[12]

Seasonal variation affects cardiovascular morbidity and mortality in the general population due to its effects on temperature and humidity. In hot weather, there is a fall in blood pressure due to vasodilatation and loss of fluid and electrolytes from the body in excessive sweating. The body has vasoconstriction and retention of fluids and electrolytes in cold weather. These are the mechanisms by which the weather affects the frequency of preeclampsia and eclampsia.[13, 14]

Sunlight affects vitamin D serum levels. Vitamin D deficiency in early pregnancy is a risk factor for preeclampsia and eclampsia in later pregnancy. Sunlight is the source of 90 % of vitamin D in the body. Pregnancies conceived in the summer months have a low incidence of preeclampsia and eclampsia.[15, 16] Seasonal changes influence maternal health globally and are particularly important for women in developing countries who suffer from anaemia, infections, preeclampsia and eclampsia.

A paper by Tina Hlimi reviewed 23 published studies. It showed a statistically significant link between these maternal disorders and seasonality in developing countries in sub-Saharan Africa, central and south Asia. Anaemia

and eclampsia are principally exacerbated in teenage primigravidas. Food insecurity, lack of antenatal care, poverty, anaemia and environmental factors play a crucial role in the predisposition of these disorders.[17]

Some authors have studied the effects of temperature and humidity at the time of conception on the frequency of preeclampsia and eclampsia later in pregnancy and concluded that eclampsia is more common in pregnancies conceived in the summer months. This is due to the direct effect of temperature and humidity on hemodynamic status.[18, 19]

Dehydration protects the brain from convulsions in hot and dry weather and promotes insensible loss of fluid from the body. Dry season-related dehydration may play a protective role in eclampsia.[20] In contrast, overhydration and hyponatraemia are well known to be associated with triggering seizures. Hyponatremia causes a direct influx of fluids into the neurons. Neurons are swollen and susceptible to injury and excitation.[21] Chakrapani and colleagues have confirmed that the incidence of hyponatremia in hospital patients is significantly high in monsoon months. Low temperature, high humidity and low barometric pressure are linked with eclampsia.[22]

A study from Texas, USA, by Kristen Wellington and Zuber D Mulla, did a retrospective analysis of hospital discharge records of 312,207 patients who delivered in Texas in 2007. Data was collected from the Texas Department of state health services. The highest prevalence was detected in the winter season (4.1%) and more so in January.[23]

Conclusion

The prevalence of hypertensive disorders of pregnancy is higher in autumn and winter. A systematic literature review was conducted to examine all the studies of seasonal variation in the prevalence of gestational hypertension, preeclampsia, and eclampsia by Megan R W. Objective was to test the hypothesis that prevalence rates are higher during winter months in non-tropical regions and during wet and humid periods in a tropical climate. Studies included were published between 1938 and 2010. Out of 60 abstracts and articles, only 20 met the final criteria. The conclusion was that prevalence of preeclampsia and eclampsia was highest in the winter season in non-tropical regions and during monsoon and post-monsoon in the tropics. Seasonal variation, infectious diseases, environmental triggers, sunlight exposure, physiological response to cold weather, health care access and nutritional deficiencies all play a role.

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ORIGINAL ARTICLE

A retrospective study on epidemiological and clinical characteristics of COVID-19 in Baluchistan (Pakistan) and its future perspectives

Sadia Sabir[1], Nazish Sabir[2], Ayesha Mushtaq[3], Merman Gul[4], Muhammad Jawad Khan[5*]

[1] Molecular Biologist, Department of Health, Provincial Public Health Reference Laboratory, Quetta, Pakistan

[2] Associate Professor, Department of Chemistry, Government Girls Degree College Jinnah Town, Quetta, Pakistan

[3] Assistant Professor, Department of Chemistry, Sardar Bahadur Khan Women's University, Quetta, Pakistan

[4] M.Phil. Scholar, Department of Chemistry, Sardar Bahadur Khan Women's University, Quetta, Pakistan

[5] Associate Professor, Department of Biosciences, COMSATS University, Islamabad, Pakistan

Author's Contribution

[1] Planning, data collection and analysis, manuscript

[2] Planning, literature review, data collection, manuscript

[3] Planning, methodology, data collection, manuscript

[4-5] Planning, questionnaire, data collection, manuscript

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Correspondence

Muhammad Jawad Khan

jawadkhan@comsats.edu.pk

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A B S T R A C T

Background: The rise of a viral respiratory sickness was recognized in China and later known as COVID-19. The current study reports the epidemiological and clinical attributes of COVID-19 in Baluchistan.

Objective: This study aimed to investigate the epidemiological parameters and route of transmission of COVID-19 positivity that will help the health department develop future strategies to handle deadly pandemics.

Methodology: This study was performed by gathering information from patients with their socioeconomics, epidemiological status, history of comorbidity, and clinical signs of the disease. The data was collected from the COVID-19 dashboard. A correlation test was applied to evaluate the connection between clinical pathological parameters.

Results: A sum of 3999 clinical records was analyzed. Total 70.8% of patients were positive, and 29.2% were negative. The most affected group was aged 22-42, however, disease severity increased with age. Most positive patients had a high fever, severe cough, sore throat, body ache, shortness of breath and comorbidity on clinical pathological grounds. The earliest reported cases of the infection were connected to travelers returning to Pakistan from Iran. The spread among men was higher as compared to women.

Conclusion: This report will display a linkage between the studies of disease transmission and clinical features which thus can be helpful to forestall the local transmission of similar infections in future. The epidemiological literature on this topic from Baluchistan is scarce.

Keywords *COVID-19, SARS-CoV-2, Comorbidities, Epidemiology, Baluchistan, Real-time PCR*

Introduction

In December 2019, the first case of a novel pathogen with respiratory side effects was diagnosed at the medical clinic in Wuhan, China. The infectious agent was identified and named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). It is an RNA virus that belongs to the COVID family and is classified in the beta genus.[1, 2] The potential onset of SARS-CoV-2 from bats could be illustrated by its proximity (88% indistinguishable) to two other SARS-like CoVs derived from bats, namely bat-SL-CoVZC45 and bat-SL-CoVZXC21.[3] The COVID-19 infection spread worldwide, affecting every mainland and sparking a global health crisis. On March 11, 2019, the

World Health Organization (WHO) declared the outbreak of COVID-19 a pandemic.

By January 23, 2023, 13,156,047,747 vaccine doses had been administered, and on January 31, 2023, WHO reported 753,479,439 confirmed cases of COVID-19, including 6,812,798 deaths.[4] On March 10, 2020, the COVID-19 National Command and Operation Cell (NCOC) of Baluchistan confirmed the first case of COVID-19 in a person returning from Iran. From January 3, 2020, to January 31 2023, WHO reported 1,576,235 confirmed cases of COVID-19 and 30,640 deaths in Pakistan. As of January 21 2023, 333,085,477 vaccine doses have been administered.[4] These statistics show that COVID-19 is still active, and its vulnerability cannot be denied. The COVID-19 infection transmits from person to person via actual contact, respiratory droplets produced by sneezing, and vertical transmission from mother to child has also been suggested.[5, 6]

Generally, it is categorized from mild asymptomatic infection to dangerous complications. Common symptoms of COVID-19 are headache, fever, shortness of breath and fatigue. Other less common symptoms include diarrhoea, migraines, and the development of sputum. Under critical conditions, this results in intense respiratory disease (ARDS), acute cardiovascular injury (ACI), auxiliary contamination, cardiovascular collapse (HF) and various organ failures.[3, 7] At the end of December 2022, the new COVID-19 variant was identified in China, devastatingly affecting the people. Later on, the same variant was identified in Pakistan. These flare at different time span exactly explain the contagious nature of SARS-CoV-2. An unexpected pandemic attack in developing countries has been challenging to deal with.

In the current study, we retrospectively analyzed the transmission design and clinical characteristics of patients with COVID-19 in the Baluchistan region. Therefore, the study investigates which gender is more affected by viruses based on their clinical attributes. The focus of the study is to help the government find successful countermeasures and control procedures.

Methodology

Study Design

A retrospective cohort study of all test screenings of COVID-19 was conducted at Provincial Public Health Laboratories Quetta. The study was designed as a situation report and was approved by Public Health Laboratory, Baluchistan Health Department, Pakistan (IRB: 1/COVID/727).

Data Collection

Coronavirus information was compiled by the Baluchistan Coronavirus Dashboard Health Department, including time span, number of test screenings, number of confirmed cases, and socio-demographic characteristics, including gender and age, etc. Data were recorded from June 2021 to September 2021, and the patients were not vaccinated.

Variables Included

Basic clinical features of patients with travel histories to China and Iran or people who had close contact with COVID-19 patients were included in the analysis. Common symptoms included fever, headache, body aches, sore throat, breathing difficulties and comorbidity.

Statistical analysis

Results were reported as numbers and rates. One-way ANOVA and linear regression tests were used to find a relationship among all clinical parameters. The $p<0.05$ was considered statistically significant. All statistical analyses were performed by programming SPSS Insights 20.

Results

A total of 3999 suspected cases were collected and used for the investigation. Each 3999 cases were screened, and 70.82 % (2833) were confirmed with COVID-19 positive. However, 29.15 % (1166) were negative. RT-PCR confirmed all suspected cases. Among 3999 patients, 70 % were positive, mainly in the 22-42 age group. The youngest patient was one year old, but the oldest was 84 (Figure 1).

Adults represented the most dynamic cases of COVID-19 and mostly lay in the 22-42 years age group; the second most affected age group was 1-21 years old; the third group ranked 43 to 63 years old, and patients above 64 account for a minimum number of cases as depicted in figure 2. One of the women was pregnant and tested positive for COVID-19, although she remained asymptomatic with no reported complications. Most males were found positive for COVID-19 compared to females.

Table 1: Association of COVID-19 infection with clinical parameters

Parameters		N	Mean	Std. Deviation	p-value
Age	Positive	2833	0.96	.81290	0.26
	Negative	1166	0.937	.88789	
	Total	3999	0.960	.83548	
First test	Positive	2833	0.497	.50008	0.05*
	Negative	1166	0.464	.49891	
	Total	3999	0.487	.49992	
Cough	Positive	2833	0.899	.30132	<0.01*
	Negative	1166	0.857	.34958	
	Total	3999	0.887	.31667	
Sore throat	Positive	2833	0.907	.29025	<0.01*
	Negative	1166	0.937	.24236	
	Total	3999	0.916	.27745	
Fever	Positive	2833	0.999	.01879	0.52
	Negative	1166	1.00	.00000	
	Total	3999	0.999	.01581	
Body ach	Positive	2833	0.810	.39202	<0.01*
	Negative	1166	0.699	.45853	
	Total	3999	0.778	.41551	
Shortness of breath	Positive	2833	0.536	.49878	0.01*
	Negative	1166	0.493	.50017	
	Total	3999	0.523	.49950	
Comorbidity	Positive	2833	0.510	.49997	0.03*
	Negative	1166	0.473	.49951	
	Total	3999	0.499	.50006	

Table 2: Correlations among all clinical characteristics

Correlation	Gender	Age	First test	Fever	Cough	Sore throat	Body ache	Shortness of breath	Comorbidity
Gender	-	0.018	0.031	0.01	.059**	.050**	.121**	.039*	.034*
Age	0.02	-	.176**	0.02	.044**	0.013	.116**	.179**	.179**
First test	0.03	.176**	-	0.015	.348**	.296**	.521**	.931**	.976**
Fever	0.01	0.02	0.015	-	.044**	.052**	0.03	-0.015	0.016
Cough	.059**	.044**	.348**	.044**	-	.376**	.458**	.316**	.357**
Sore throat	.050**	0.013	.296**	.052**	.376**	-	.123**	.262**	.303**
Body ache	.121**	.116**	.521**	0.03	.458**	.123**	-	.515**	.534**
Shortness of breath	.039*	.179**	.931**	0.015	.316**	.262**	.515**	-	.954**
Comorbidity	.034*	.179**	.976**	0.016	.357**	.303**	.534**	.954**	-
**. Correlation is significant at the 0.01 level (2-tailed).									
*. Correlation is significant at the 0.05 level (2-tailed).									

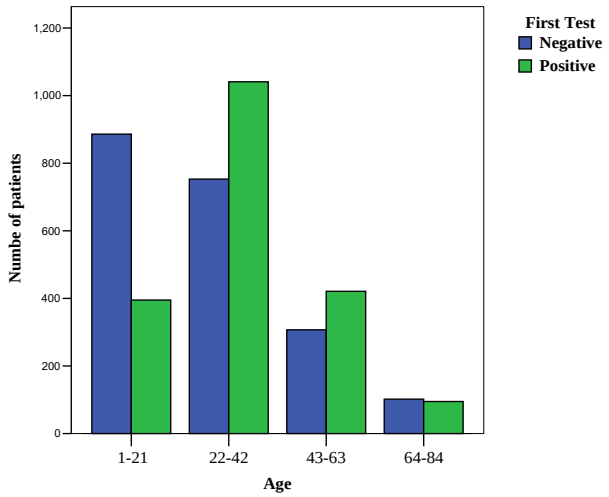

Figure 1: Distribution of age in years among total COVID-19 positive and negative cases

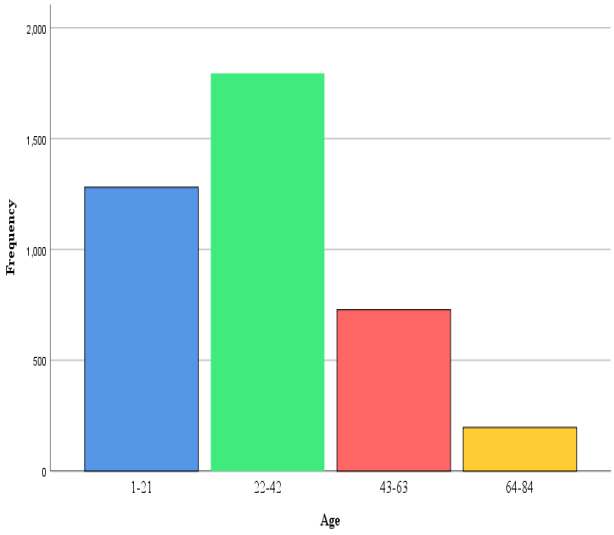

Figure 2: Distribution of age in years among COVID-19 patients

In the current consensus, a linear regression test was performed among all clinical parameters and a strong positive association was observed among all clinical parameters, e.g., sore throat, cough, body aches and shortness of breath and comorbidity. However, both men and women lacked a positive association with fever. The correlations** were highly significant at the 0.01 level, whereas the correlations* were significant at the 0.05 level (Tables 1 and 2). The test results correlated significantly with cough, sore throat, body aches, shortness of breath and comorbidity. Comorbidity correlated strongly with the patients' first test and shortness of breath.

Discussion

It was suggested that SARS-CoV-2 was passed from a bat to a human when it was consumed as food, thus making it a zoonotic illness with potential human-to-human transmission through coughing and nasal droplets.[8, 9] Due to these factors, it quickly spread across the globe, disregarding borders. The first case in the US was reported on January 19, 2020, and France reported its first on January 24, 2020. However, the first case in Pakistan was reported later than many other countries, on February 24, 2020.[10, 11]

Despite the global pandemic, the public authority of Pakistan took positive steps to prevent the spread of COVID-19, which may account for the lower number of cases and deaths in the country. Furthermore, this may be partially attributed to environmental factors or the innate immunity of the people. Additionally, the timely availability of higher medication dosages may help protect the population, thus contributing to a lower morbidity and mortality rate.[12] SARS-CoV-2 is a highly pathogenic strain it spreads all over Pakistan. However, the Baluchistan region reported fewer cases than other thickly populated areas of Pakistan. One possible reason could be the lower testing limit of Baluchistan compared to the rest of Pakistan.

The authors believe the total number of COVID-19 cases is probably higher yet under-reported because of the troubles in recognizing mild and asymptomatic cases present locally. COVID-19 can cause hospitalization and even death in young and middle-aged adults. It has caused the most severe health problems in adults over 60 and a higher mortality rate in patients over 80. Comorbidities, e.g., diabetes, hypertension, heart disease or other chronic conditions, can cause more intense manifestations and complications of the disease. Also, older people are more susceptible to infections due to gradually losing immunity. According to our findings, people over 60 were the most vulnerable age group, as documented by other studies.[13, 14] Children and young adults were less susceptible to disease, whereas the middle age group with the highest community exposure appeared severely affected. With increasing age, the severity of infection stepped up.

According to a global investigation, females and kids are less prone to infection than males. Similar findings

were reported in our study because in Pakistan, mainly males have more public exposure than females and kids. Likewise, reports from China and Italy demonstrate that females and kids were less affected, particularly in severe cases.[14] The actual cause of this deviation is not known yet. However, research was conducted to investigate the association of gender with infection. Both male and female mice were exposed to SARS-CoV and MERS-CoV, which showed that male mice were more susceptible to infection than female mice.[15]

To date, there is no reliable evidence of the influence of gender on disease vulnerability. Further investigations are required to determine the actual cause. Our results indicated that most patients with COVID-19 in Baluchistan were asymptomatic. It could be risky as the asymptomatic patients infect many people without identification. Another research conducted in Iceland found that 43% of members have positively reported no symptoms.[16, 17] According to the WHO, more than 70,000 early cases of COVID-19 in China were identified as having the same symptoms as SARS-CoV and MERS-CoV, including fever (88%), dry cough, sore throat (68%), fatigue (38%) and diarrhoea (4%).[18, 19] SARS-CoV2 usually attacks the respiratory system and can cause severe shortness of breath, heart damage, or chronic bacterial infections. The current consensus also reported the same results.

Fever, cough, fatigue, sore throat, shortness of breath, comorbidities, and body aches were among the most frequently found symptoms, and all these factors have a strong positive association with gender. Previous research has also documented similar results. The clinical side effects of 100 patients admitted to an emergency clinic in Karachi showed the same symptoms as dry cough, fever, comorbidity, sore throat and shortness of breath.[20, 21] Other studies also demonstrated similar signs and symptoms.[22, 23] Total of 4.12% of subjects remained asymptomatic. Shockingly, 6.70% of patients showed a lack of sense of smell and taste with varying side effects, and this is a strong indicator of COVID infection.[24, 25]

There may be a connection between the Coronavirus and the human population and animals. Some animals were documented positive for SARS-CoV-2, but the Coronavirus did not affect chickens and ducks under test conditions. Interspecies transmission of the Coronavirus has been persistent and should be addressed after various investigative studies.[26]

Conclusion

COVID-19 is not only a health crisis but also an economic threat. It has been moving like a wave that has caused multiple deaths and devastated the world economy. In Baluchistan, the highest morbidity rate was observed in men than in women and children; the mortality rate was higher in older people. Strict measures must be taken to avoid the plausible effects of a future deadly epidemic in Baluchistan. We must improve diagnostic and therapeutic strategies according to standard protocols to do this.

Recommendations

Countries with poor health infrastructure and unreadiness to deal with this pandemic faced enormous hurdles. The main obstacles hampering Pakistan's ability to respond to the current pandemic are the country's poor infrastructure and financial constraints. The government should establish contact with the private sector to finance public health measures. The biosafety protocols have been completely revised in line with the new WHO Laboratory Biosafety Manual.

SARS-CoV-2 must be processed under controlled measures as it is a highly pathogenic human pathogen of risk group 3 (RG3). To maintain biosafety and biosecurity, the WHO and the United States CDC (Center for Disease Control and Prevention) have proposed BSL3 laboratories for COVID-19. Unfortunately, Baluchistan lacks BSL3 laboratories, so the work is carried out in BSL2+ facilities, and the Baluchistan government deserves credit for its efforts during the pandemic. However, to cope with such a deadly epidemic in the future, more significant steps are required, so upgrading the laboratories to the BSL3 level is urgently needed. To help the administration of Baluchistan, national and international organizations must come forward.

Numerous small compounds and antiviral drugs have been shown to block the effects of COVID-19 and MERS-CoV in preclinical testing, but human clinical trials have yielded disappointing results. Repurposing currently available drugs to treat this pandemic is one possibility, as all coronaviruses, including SARS-CoV-1, MERS-CoV,

and SARS-CoV-2, share structural and genetic similarities. On the other hand, antibody, mRNA, protease and replicate targeting drugs, viral glycoprotein, and receptor targeting therapies are some of the emerging methods for the prevention and treatment of SARS-CoV-2.

However, testing and developing novel therapeutic approaches takes much time. The ongoing study is one of the primary investigations to depict the epidemiological picture of the Coronavirus in Baluchistan to draw the attention of higher authorities to preliminary strategies for all types of COVID-19 strains and virus outbreaks. As a country with lower wages in the middle, Pakistan faces many relocations, from inadequate health facilities to poor socio-economic conditions. Our study can help to identify and develop a response that can alleviate the rapid onset of the disease.

Further research is required in the diagnostics, vaccines and therapeutics section to stop the spread of infection and advance treatment strategies most productively. The coronavirus pandemic is a test for the world and Pakistan. It is essential to learn the lesson and develop preparedness further to anticipate any deadly pandemics in the future. In the future, more skillful use of technology and artificial intelligence could be used to predict and demonstrate disease spread. The need of the hour is the more special order of preparedness, scientific advice from time to time, and response to infectious disease flare-ups, accompanied by a significant increase in funds.

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REVIEW ARTICLE

The cardiovascular system's Renin-Angiotensin-Aldosterone System (RAAS)

Lamiaa Saoud Abbod[1*], Fatima Amer Abd Algabar[2]

[1] Technical Demonstrator, Department of Nursing Technologies, Baquba Technical Institute, Middle Technical University, Diyala, Iraq

[2] Technical Demonstrator, Department of Nursing Technologies, Baquba Technical Institute, Middle Technical University, Diyala, Iraq

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Correspondence

Lamiaa Saoud Abbod

lamiaasaoud67@gmail.com

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A B S T R A C T

The renin-angiotensin-aldosterone system (RAAS) has a noteworthy part in triggering, and inflammation is maintained by its physiological agents. A crucial mechanism for the initiation and headway of CVD, including Hypertension and atherosclerosis, is inflammation. In addition to its primary function in controlling blood pressure and its contribution to Hypertension, RAAS has pro-inflammatory and profibrotic cellular and molecular effects. Cardiovascular and renal disorders can be treated more effectively by hindering RAAS. Proof recommends that RAAS inhibition enhances vascular remodelling and gets better CVD sequels. Lower levels of oxidative stress and endothelial dysfunction, vascular inflammation, and favourable effects on endothelial progenitor cell regeneration are likely the causes of RAAS inhibition's sound vascular effects.

Keywords: *Renin-Angiotensin-Aldosterone System (RAAS), Hypertension, Atherosclerosis, Vascular Remodeling, CVD*

INTRODUCTION

Among the most crucial hormonal systems, the renin-angiotensin-aldosterone system Governors blood pressure, melted amount, and the balance of sodium and potassium to control the activities of the heart, kidneys, and adrenal glands.[1] More than a century ago, the classical RAAS system was found. 1934 Goldblatt et al. confirmed a Renin association between kidney blood pressure and activity.[2] At that juncture, numerous trial inquiries must be conducted to pinpoint the RAAS's constituent parts and their function in controlling blood pressure. A variety of cardiovascular disorders cardiovascular diseases (myocardial infarction, stroke, and congestive heart failure), renal malady, and CVD (Hypertension, atherosclerosis, and left ventricular hypertrophy) are all triggered by aberrant RAAS activity.[1]

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RAAS:

Prorenin, a torpid preprohormone that is later renovated into renin, an active proteolytic enzyme, before being released into circulation, takes place in the renal glomerulus' afferent arterioles.[3, 4] Proteolytic and no proteolytic processes hew prorenin to the present renin in the bloodstream. Angiotensin I is produced by active renin's reaction with its substrate, angiotensinogen (Ang I). Angiotensin-converting enzyme (ACE) breaks down Ang I to fabricate physiologically active Angiotensin II (Ang II). The primary RAAS effector, Ang II, conveys its actions through the type 1 Ang II receptor (AT1R). Little research points to additional prorenin and renin receptors in the heart, kidney, liver, and placenta.[5] Other investigations indicate that visceral and subcutaneous adipose tissues have renin receptors, indicating a local generation of Ang II. Prorenin and renin receptor activation activate a signaling pathway connected to a mitogen-activated kinase (MAPK) and extracellular signal-regulated kinase (ERK1/2).[6] Since renin regulates the rate-limiting stage of RAAS, the notion of impeding renin to reduce RAAS was proposed in the middle of the 1950s. Nevertheless, the stayed of renin inhibitors was a delayed and challenging procedure.[7]

Cardiovascular Disease and Inflammation

Numerous cardiovascular diseases, including Hypertension, atherosclerosis, restenosis following balloon angioplasty, nephropathy, and cardiomyopathy, are primarily attributed to inflammation in their onset, progression, and development.[8] A common illustration of how irritation drives the onset of cardiovascular disease is atherosclerosis, caused by stirring cytokines activating endothelial cells. Cardiovascular menace elements like Hypertension, diabetes, or obesity have been linked to endothelium dysfunction brought on by inflammation-induced injury.[9]

Markers of Inflammation

In practically all cell types, polyp necrosis element alpha (TNF) is a crucial pro-inflammatory cytokine that controls the articulation of several genes involved in soreness, oxidative stress, and anti-apoptotic signing lanes.[10] Therapeutic TNF signaling inhibition has been offered in dealing with several inflammatory disorders, especially rheumatoid arthritis and bowel disease. Aberrant TNF signaling promotes the progress of unreasonable settings, such as cardiovascular disease. By generating superoxide radicals, TNF reduces the endothelium-dependent nitric oxide (NO) mediated vasorelaxation in coronary or carotid arteries.[11] cardiovascular diseases are more likely to develop in patients with elevated ranks of circulating TNF. TNF promotes the invention of cell adhesion molecules (CAM), monocyte chemoattractant protein-1 (MCP-1), and interleukin-6 (IL-6) in endothelial cells [21]. Mice lacking TNF are less likely to experience intimal hyperplasia following carotid artery damage, whereas mice with higher levels of TNF expression experience worsening pulmonary Hypertension.[12] Vascular remodeling is significantly influenced by TNF mediated inflammation. Rats' carotid artery post-injury media remodeling and neointima development are prevented by inhibiting circulating TNF, but human carotid artery smooth muscle cells invention to TNF by increasing cell proliferation. It has been demonstrated that inhibiting TNF increases endothelium function by promoting the regeneration of endothelial cells. Interleukin-1 beta (IL-1), interleukin-6 (IL-6), TNF, and MCP-1 are vascular inflammatory mediators expressed in endothelial cells and other cell types. NF-B, a pro-inflammatory factor downstream of TNF, controls their expression.[13]

Following vascular damage, activated NF-B promotes the proliferation of vascular smooth muscle cells and is a critical factor in neointima hyperplasia.[14] C-reactive protein is an additional indicator of redness (CRP). The acute-phase response is thought to be typified by CRP, a charity that foretells the risk of cardiovascular events. [14] CRP is also expressed in other cell types, including smooth muscle and the endothelial cells of atherosclerotic arteries. Vascular disease is mediated in part by CRP. Studies conducted in vitro have revealed that CRP upregulates AT1R, impairs endothelial progenitor cell differentiation and function, and has pro-inflammatory and prothrombotic effects.[14-16] Neointima development in damaged arteries is significantly aided by CRP's activation of the classical complement signaling cascade.

RAAS and Vascular Inflammation

Vascular inflammation and remodeling are initiated mainly and maintained by RAAS. Cardiovascular disease

progresses due to impaired endothelial function brought on by vascular inflammation. A defective endothelium is leaky, promotes inflammatory cell migration into the arterial wall, and increases the rapid growth of smooth muscle cells, all of which reduce vascular function and raise the danger of tissue damage and cardiovascular disease. An endothelium that isn't working properly creates an inflammatory environment that encourages the attachment and recruitment of inflammatory cells, which are notorious and designated crucial in the elaboration of atherosclerosis. An association relating high blood pressure to atherosclerosis through Ang II-mediated inflammation is becoming more evident. Acute administration of Ang II in rats significantly increases leukocyte adhesion.[17]

Studies on humans and animals demonstrate that Ang II causes pro-inflammatory reactions in the kidney, heart, and arteries by controlling cytokine and chemokine expression. Ang II activates NF-B and causes the production of IL-6.[18] Atherogenesis is an inflammation-mediated process initiated and progresses due to Ang II. By recruiting inflammatory cells, Ang II creates a positive feedback loop in wounded arteries, producing additional Ang II and vascular inflammation.[19] A strong prooxidant, Ang II. Superoxide anions are produced due to Ang II, and prooxidant NADH/NADPH signaling is also activated. NO protects the cardiovascular and renal systems. Numerous effects of NO on the vasculature include leukocyte adherence to endothelium inhibition, platelet aggregation and adhesion inhibition, and vasodilatation of all types of blood arteries. Additionally, NO reduces oxidative stress and suppresses the proliferation of vascular smooth muscle cells, mitogenesis, and DNA synthesis.[20]

NO bioavailability depends on eNOS activity, and essential Hypertension is linked to decreased eNOS activity. Aldosterone is another hormone that the RAAS uses to mediate its pro-inflammatory and profibrotic effects. Aldosterone causes cardiac fibrosis in conjunction with macrophages and contributes to tissue ischemia and organ fibrosis.[21] Aldosterone influences vascular remodeling, insulin resistance, and atherosclerosis processes. Aldosterone changes insulin signaling in vascular smooth muscle cells by upregulating the IGF1R and hybrid receptors' expression and modifying membrane shape via tyrosine kinase receptors.[22] Rat aorta oxidative stress is induced by chronic aldosterone infusion, and the MR antagonist spironolactone decreases reactive oxygen species production.[23]

RAAS Blockers and Vascular redness

This document aims to discuss the upshots of RAAS blockers on vascular soreness and subsequent cardiovascular events. Recent clinical studies have found that RAAS blockers, such as angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs), canister shrink the risk of vascular inflammation and subsequent cardiovascular events. [24] However, the exact mechanisms these drugs reduce inflammatory responses are still largely unknown. This paper will discuss the research available and provide insights into the potential effects of RAAS blockers on vascular inflammation and subsequent cardiovascular events.[25]

The benefits of RAAS blockers in treating vascular inflammation are well-documented. RAAS blockers are a class of drugs that block the action of the renin-angiotensin-aldosterone system, thus preventing the release of vasoconstrictor hormones and decreasing inflammation. In addition, RAAS inhibitors may reduce the risk of developing vascular complications by tumbling inflammation in the affected area. Furthermore, RAAS blockers can help to improve blood flow and reduce oxidative stress, which can help to reduce the risk of stroke and heart attack.[26]

Direct Inhibitors of Renin (DRIs)

By preventing renin's enzyme activity, DRIs prevent RAAS. The oral direct renin inhibitor aliskiren, a recently licensed DRI, reduces blood pressure by obstructing the RAAS's rate-limiting phase. Andersen et al. and others. Aliskiren is well-tolerated by the endothelium. In type I diabetic patients, it enhanced endothelial function without lowering blood pressure.[27] In a transgenic mouse model, aliskiren alone or combined with atorvastatin decreased atherosclerosis onset and progression by decreasing monocyte adhesion and MCP-1 levels.[28]

Potential Inhibitors and the (pro)renin Receptor

Inhibitors of this receptor can be used as therapeutic agents for various disorders, such as Hypertension and diabetes. Recent analyses have indicated that the prorenin receptor is essential for regulating blood pressure and may be a target for new treatments. Various types of inhibitors

can be used to target the prorenin receptor, from small molecules to natural products. Recent analyses have highlighted the prorenin receptor (PRR) potential as a potential renin-angiotensin system (RAS) inhibitor.[29] The RAS is a brigadier hormonal system in mammalian physiology and is labyrinthine in the instruction of cardiovascular and renal functions. PRR is believed to be a key inhibitor of RAS activity, potentially offering novel therapeutic targets for treating Hypertension, stroke and cardiovascular diseases. By binding to PRR, prorenin may be able to reduce the activity of the RAS, leading to decreased blood pressure and improved cardiovascular health.[30]

Inhibitors of the ACEIs

ACEIs have been widely used to treat cardiovascular diseases, Hypertension, cardiac botch, and coronary artery infection. ACEIs inhibit the endeavor of angiotensin-converting enzyme, which is necessary for the production of angiotensin II, an important hormone which regulates blood pressure. By spoiling the realization of angiotensin II, ACEIs reduce blood pressure and improve symptoms of cardiovascular diseases. In addition to their effects on cardiovascular diseases, ACEIs have been shown to have other benefits, such as reducing the gamble of myocardial infarction and fondle.[31]

Angiotensin Receptors Blockers (ARBs):

RAAS blockade with ARBs has proven to improve endothelial function and inflammation. The anti-inflammatory action of ARB candesartan is mediated via calming of the inspiring process toll-like receptors 2 and 4 (TLR2 and TLR4). According to investigations done in vivo and in vitro.[32] TLRs have been linked to the onset and evolution of cardiovascular disease. TLR4 participates in blood pressure control and a slight resistance artery vessel constriction in animal models of Hypertension. Irbesartan, an ARB, has been demonstrated in studies on hypertension patients to lower CRP, ICAM-1, IL- 6, and 8-isoprostane, a measure of levels of oxidative stress, as well as to enhance vascular responsiveness and endothelial function. [33] In mediating endothelial dysfunction, it is inhibited in its function. Both are factors in the development of vascular inflammation and vascular incidents.

Studies conducted in the lab and on animals have revealed that ARB Olmesartan blocks the migration of aortic vascular smooth muscle cells caused by Ang II, preventing vascular remodelling.[34] The use of ARBs in treating atherosclerosis and coronary disease is advantageous. Patients with atherosclerosis and healthy endothelial function benefit from losartan medication regarding flow-mediated coronary artery disease.

Mineralocorticoid Receptor Antagonists (MRA):

Independent of the effects of blood pressure effects of renal MR, dysregulated mineralocorticoid system signaling has an impact on Hypertension, atherosclerosis, and cardiac failure.[35] In patients with cardiovascular disease and danger elements, abnormally activated MR adversely regulates endothelial function. Eplerenone and spironolactone, two commercially available antagonists, are efficient treatments for heart failure with high blood pressure.[36] They work by inhibiting aldosterone actions at the level of MR. MR found in vascular smooth muscle cells, EL cells, and cardiomyocytes mediate the impact of aldosterone on the cardiovascular system. According to studies, MR activation triggers several waving trials in the cardiovascular system along with oxidative stress, inhibits vascular lessening, and results in vascular irritation, fibrosis, and remodelling.[37]

Novel antagonists of the mineralocorticoid receptor:

Since only a few MRA have received clinical approval (spironolactone, eplerenone, and canrenone in the US and Europe), research is now being done to create new MRA. However, only a few newly identified compounds were developed for medical training due to MR structure-based drug design research, which has produced a few new MRA candidates. One of these novel MRAs, PF-3882845, dramatically decreased urine albumin and preserved kidney; these outcomes enabled this novel MRA to be used in ongoing clinical investigations.[38]

The MR binding selectivity of other latest MR antagonists, including dihydrofuran-1-one and dihydropyran-2-one, is highly promising in vitro experiments. However, BR-4628, a novel selective nonsteroidal molecule recently discovered, has demonstrated significant efficacy and discernment on behalf of MR in vivo and in vitro conclusions.[39]

Aldosterone Synthase Inhibitors

The creative substitute method to MRA for limiting the effects of aldosterone is to reduce Aldosterone production

at the enzyme stage, Aldosterone production (AS), CYP11B2. The newest treatment method to minimise aldosterone synthesis is aldosterone synthase inhibitors (ASI).[40] While decreasing Fadrozole 286A (FAD 286A) enhanced plasma renin hobby, cardiac hypertrophy, and cardiac rehab in animal models, which was evidenced by dose-dependently block Ang II Conjugated aldosterone blend in human adrenocortical carcinoma cells.[39]

Revascularization and RAAS

Ang II also causes thrombosis, vessel modification, and plaque rupture. It takes the expression of the fundamental fibroblast growth factor (bFBS), changing development factor-1 (TGF1), and the growth factor insulin (IGF) for Ang II to encourage vascular remodelling.[37] The enhanced migration of vascular cells and altered extracellular matrix composition caused by Ang-II mediated vascular remodeling. Changes in blood artery form and function, particularly in small resistance blood arteries, exacerbate the side effects of high blood pressure. Additionally, tiny blood vessels remodel before left ventricular hypertrophy, thickening of the mediastinum in the carotid arteries, and elevations in microalbuminuria levels. People with Hypertension have tiny resistance arteries with smaller lumens and exterior diameters.[40] Reduced amounts of vasodilators and higher awareness of Ang II and associated routes for transferring signals are linked to changes in tiny arteries' function.

The growth factor Ang II also controls the differentiation, hypertrophy, and death of cells. Vascular smooth muscle cells' multiplying and hypertrophy are the causes of the Ang II-induced remodeling upshots in vascular remodeling. The proliferation versus hypertrophy impacts of Ang II depends on the kind of cell and the genes that control the cell cycle. TGF1-mediated signaling from Ang II causes cardiomyocytes to hypertrophy, and blocking the TGF1 receptor reverses this effect. Cardiomyocytes enlarge as a result of Ang II. [38] Atherosclerosis and post-angioplasty neointima hyperplasia are vascular remodeling diseases where the systemic and local renin-angiotensin systems play a significant role.[41]

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CASE REPORT

Hyper Immunoglobulin E (IgE); an immune deficiency (Job Syndrome)

Saqib Ismail[1*], Fatima Khurshid[2]

[1] Head of Department, Department of Pediatric Surgery, DHQ Hospital Mirpur, AJK, Pakistan

[2] Medical Doctor, Department of Medicine, Mohi-ud-Din Islamic Medical College, Mirpur AJK, Pakistan

Author's Contribution

[1] *Manuscript writing*

[2] *Data collection and compilation*

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Correspondence

Saqib Ismail

saqib.dr@gmail.com

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A B S T R A C T

Hyper-IgE Syndrome (HIES), also known as Job Syndrome. HIES is a rare genetic disorder that affects the immune system and can lead to various health complications. The text mentions that the cornerstone of HIES therapy is proper skin care, infection prevention, and aggressive infection treatment. Treatments for HIES can include antibiotics that target S. aureus, typically used to reduce the incidence of pneumonia and the risk of lung damage. Skincare routines can involve bleach baths or chlorhexidine washes, oral anti-staphylococcal prophylactic antibiotics, and other treatments to avoid abscesses. Antifungal prophylaxis may be beneficial for HIES patients who have chronic Candida infections. Commonly occurring hypertension should be treated because it may be related to vascular problems. Defects in antibody synthesis can vary, making it difficult to provide general recommendations for immune globulin replacement in HIES. However, anti-staphylococcal prophylaxis is probably necessary for all individuals.

Keywords: *Hyper-IgE Syndrome, Splenic Abscess, STAT3 mutation, Eczema, Recurrent Infections*

Introduction

Eosinophilia, eczema, and recurring skin and lung infections are the hallmarks of the immunological deficit known as Job Syndrome, also known as High Immunoglobulin E (IgE) syndrome. Job syndrome is uncommon; it affects about one in one million people annually.[1] IgE levels are also high in primary childhood and begin early when two patients with eczema, recurring pulmonary infections, and cold lung abscesses were first diagnosed with "Job syndrome" in 1966, David et al. Later, in 1972, Buckley et al. found a connection between this syndrome and elevated serum immunoglobulin E (hyper-IgE) levels and behavioral characteristics known as HIES (Hyper Immunoglobulin E Syndrome). Almost two-thirds of individuals with job syndrome have a STAT3 gene mutation.

Case report

A 9-year-old male boy who had previously experienced bleeding wounds on the left anterolateral side of his chest and belly came to see us. Also, there was a six-month history of abdominal pain, fever, cough, vomiting, and various skin abscesses that flared up and down. History of therapy at many facilities without receiving ongoing care. A large infected ulcer measuring 20 x15 cm was discovered during an examination, with serous and purulent drainage, necrotic cheese debris, and the anterolateral side of the left chest and belly.

There were visible scars from previously treated abscesses on the hands and forearms. X-rays of the chest and abdomen showed haziness in the lower left lung. An uneven necrotic fluid attenuated region is visible in the CECT abdomen and chest. After receiving conservative

care and multiple debridements, the patient's wound began to heal. She was then discharged and gradually resumed oral feeding, but a few months later, she presented with nearly the same complaints. This time, CECT abdomen and immunoglobulin levels were checked because immunodeficiency was suspected, and the results revealed high IgE levels along with normal IgG, IgA, and IgM levels.CECT abdomen revealed a splenic abscess and localized collection at the perigastric region. A hyper IgE with skin lesions was diagnosed with job syndrome. IVIG was used to treat the patient. An exploratory laparotomy was planned. The peri-gastrin necrotic tissue was removed, a jejunostomy was made, and the splenic abscess was cleaned up. The culture of pus and necrotic tissue showed a fungus infection which was handled appropriately. The whole area healed without needing a skin graft, thanks to multiple wound debridements and dressings with vinegar, coco powder, and ginger.

The patient was advised to take care of his skin, use antimicrobial prophylaxis, and seek quick infection treatment. Pneumococcal vaccination was also administered to the patient. The patient's abdominal scar is healthy, with no new skin infections over the past year.

Figure 1: A Journey to Recovery: A Patient's Triumph over Job Syndrome Skin Infection

Discussion

An extremely rare immunodeficiency known as the hyper-IgE syndrome with recurrent infections is characterised by recurring cutaneous and lung abscesses and serum IgE levels that are abnormally raised. There have been identified skeletal and facial characteristics. Because it frequently results in abscesses, eczematoid rashes that last for a long time, and extremely high blood IgE levels, the hyper IgE syndrome has been predominantly classified as an immunodeficiency condition.[3]

A specific autosomal dominant genetic mutation in the STAT3 gene causes Job syndrome. The immune system and healing processes both involve STAT3. This gene's mutation will increase the amount of immunoglobulin E B cells produce, reduce their ability to be modulated by IL-6, IL-10, and IFN-gamma, and impair neutrophil chemotaxis. IL-10's lack of anti-inflammatory properties likely causes the inadvertent inflammatory response in Job syndrome patients. The absence of IL-6 causes a shortage of Th17 cells in Job syndrome because IL-6 is essential for developing Th17 cells. In the fight against the CD4 + Th17, cells are crucial. Autosomal-dominant and autosomal-recessive are two distinct variants of the condition that have been identified. Several skeletal, connective tissue, facial, and dental abnormalities are associated with the autosomal-dominant variant of the condition but not with the recessive form.

Chronic eczematoid eruptions, recurring skin and bacterial lung infections, and mucocutaneous candidiasis are the main immunological symptoms. These patients frequently develop cold staphylococcal skin abscesses with minimal to no inflammation. The skin, mucous membranes, and nails are frequently affected by candida infections. The most frequent side effects are upper airway infections, which manifest as paranasal sinusitis, exudative otitis media, otitis externa, mastoiditis, or respiratory tract infections. S. aureus, including methicillin-resistant strains, and rarely H. influenzae and Streptococcus pneumoniae are frequently to blame for severe reoccurring respiratory infections. The leading cause of death in HIES is pulmonary sequelae, which continuously contribute to the development of chronic respiratory insufficiency. Non-immunological Characteristics include distinctive face

characteristics that first show in early adolescence or earlier.[2, 4]

Reviewing documented lymphoma cases in people with Job's syndrome reveals a higher relative risk, particularly for class C Hodgkin and mature B cell lymphomas. [5] Proper skin care, infection prevention, and aggressive infection treatment are the cornerstones of HIES therapy. Although HIES patients may not exhibit the typical symptoms of infections, such as fevers, chills, or rigours, it is critical to take a thorough medical history, perform a physical examination, and use the right imaging to detect infections.

To reduce the incidence of pneumonia and the risk of parenchymal lung damage, prophylactic antibiotics targeting S. aureus are used (such as trimethoprim/sulfamethoxazole). To treat eczematoid dermatitis and avoid abscesses, skin care routines typically involve bleach baths or chlorhexidine washes, oral anti-staphylococcal prophylactic antibiotics, and these other treatments. Antifungal prophylaxis may benefit HIES patients with onychomycosis or other chronic Candida infections despite not being commonly administered. Aspergillus-treating antifungal medications. Commonly occurring hypertension should be treated because it may be related to vascular problems.[6, 7]

Defects in antibody synthesis can vary. 8 It has been difficult to provide general recommendations for immune globulin replacement in HIES due to this inherent variance in the B cell repertoire. Receivers of immune globulin are said to have fewer infections in certain publications, which is to be expected in some circumstances. Tests on antibody responses and replacement options in cases where deficiencies are evident seem reasonable. Anti-staphylococcal prophylaxis, however, is probably necessary for all individuals.[9-11]

Conclusion

A good collaborative effort of surgeons, physicians and pathologists can overcome any problematic diagnosis and management challenge.

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CASE REPORT

Trichobezoar: A case report of a hairball in the stomach

Fatima Khurshid[1*], Muzzamal Hussain[2], Ans Abdul Razzaq[3]

[1] Medical Doctor, Department of Medicine, Mohi-Ud-Din Islamic Medical College, Mirpur AJK, Pakistan

[2] Post Graduate Trainee, General Surgery, DHQ Hospital Mirpur, Mirpur AJK, Pakistan

[3] Dental Surgeon, Department of Dentistry, Islamic International Dental College, Islamabad, Pakistan

Author's Contribution

[1] Data collection, Scientific advisor
[2] Writing & technical editing
[3] Analysis & interpretation

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Correspondence

Fatima Khurshid
fatimakhurshid61@yahoo.com

A B S T R A C T

Trichobezoar is an underdiagnosed condition that should be considered in children and teenagers, particularly girls. According to a late diagnosis, trichobezoars can result in gastrointestinal bleeding or perforation. In this report, we discussed a 14-year-old girl who presented with severe abdominal pain with a well-defined mass in the Epigastrium; a CT scan revealed a giant mass with stomach distension which was removed through Gastrotomy. Gastric bezoars that are misdiagnosed could have life-threatening effects. Effective screening is necessary for early diagnosis. It is crucial to receive medical counselling to avoid a recurrence of bezoar.

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Introduction

A hairball in the proximal gastrointestinal system, known as a trichobezoar, is a rare illness that usually affects young females. Because of its flat surface, human hair slows peristalsis and digestion. As a result, it accumulates in the stomach's mucosal folds.[1] The first reported occurrence of human trichobezoars was described in 1779.[2] A bezoar is a food or foreign particle buildup in the gastrointestinal tract. Based on the primary constituent, it can be classified as trichobezoar (hair), phtyobezoar (plant material), Lactobezoar (concentrated milk formula), and Pharmacobezoar (mixed medicine bezoars). Still, it can also fall into other categories, such as fungal aggregation, food boluses, chemical concretions, and foreign materials.[3, 4] Continuous hair intake can impact hair, mucus, and food material. Over time, continuous hair ingestion can affect hair, mucus, and food particles in the stomach.[4]

Typically, trichobezoars must be removed through Gastrotomy while treated with broad-spectrum antibiotics.[5] It is a rare condition affecting less than 1% of the population. Teenage females aged 13 to 20 years old with long hair who have trichotillomania (compulsive pulling out of hair) or trichophagia (compulsive eating of hair) account for 90% of trichobezoar cases. [6] In this report, we looked at the case of a 14-year-old girl who arrived with severe stomach pain and a well-defined lump in the Epigastrium.

Case report

A 14-year-old female complained of abdominal pain, anaemia, loss of appetite, and body weakness during the previous six months. The patient was skinny, pallid, and well-oriented on physical examination, with normal baseline values. Abdominal examination revealed an 8x9cm immobile intra- abdominal hard mass in the Epigastrium. Physical examination revealed no additional significant findings. The contrast-enhanced CT scan of the abdomen revealed a distended stomach with a large mass lesion seen, confirming the shapes of the gastric fundus, body, and pyloric antrum, as well as the pyloric canal of the stomach, measuring approximately 7.4 x 7.6 x 26.4 cm (AP X TR X CC) and extending to the proximal part of the duodenum.

It has a whorled appearance, fat attenuation regions, and a large distal ileum Lumen. Differential Leiomyosarcoma, gastric malignancy, and gastric trichobezoar were diagnosed. These findings prompted the decision to do surgery. She had exploratory laparotomy and Gastrotomy while under general anaesthesia. A huge trichobezoar (Figure 1) was removed during an upper midline exploratory laparotomy with Gastrotomy. The Gastrotomy was closed in two layers, and the abdomen was sealed with drainage. The patient recovered well after surgery, was able to eat on the fifth postoperative day, had the skin stitches removed on the tenth postoperative day, and was discharged in good health. The psychiatric staff agreed. Before being discharged, she was advised for psychiatric follow-up to prevent recurrence.

Figure 1: Following its removal, A Trichobezoar.

Discussion

Trichobezoars have been related to psychiatric diseases, most notably trichophagia and trichotillomania (the desire to pull out and swallow hair), which are more common in young women. Trichophagia is thought to be practised by only 5-10% of trichotillomania patients. Although the underlying processes of trichotillomania and trichophagia are unknown, pulling out and consuming hair are associated with feelings of fulfilment and alleviation from negative emotions. Compared to adults seeking treatment, childhood behavioural therapy or response prevention has been shown to have a lower likelihood of recurrence.[5]

Indigestion, early satiety, abdominal pain, nausea, vomiting, digestive bleeding, iron deficiency anaemia, and weight loss are characteristic indications and symptoms of gastric trichobezoar.[6] Physical examination typically indicates a palpable moveable abdominal mass (70%) and hair loss on the head, brows, and eyelashes. Long-term gastric bezoars can induce deadly complications such as obstruction, perforation, haemorrhage, intussusception, peritonitis, ulceration, and obstructive jaundice.[7] Upper endoscopy, Ultrasound, and CT scans are all diagnostic imaging procedures. While the Ultrasound is accurate in some instances, the CT scan is more accurate. An endoscopy or even a basic radiograph might be used to make a diagnosis swiftly. We performed conventional CT scans to diagnose and confirm our situation.[4]

The trichobezoar is intended to be removed through open, laparoscopic, or endoscopic surgery. Upper endoscopy is not recommended in these situations since it has a lower success rate and a higher risk of airway obstruction and respiratory arrest while being less invasive and expensive. An examination of seven cases of gastric bezoars found that most cases are treated with open surgery; all patients had exploratory laparotomy.[8] Even though the first laparoscopic bezoar extraction was performed in 1998, only a few successful instances are described in the literature. In our situation, the patient had an exploratory laparotomy with a gastrotomy.[7]

Three strategies are discussed in the literature. Don et al. first described constructing an intra-gastric port by inserting a 10-mm port into the gastric wall and then withdrawing the specimen with a gastroscope.[9] Second,

Kanetala et al. developed a similar procedure that entailed cutting the bezoar into small pieces using two stomach ports and extracting them via gastroscopy; both methods take time.[10] Shami et al. described a gastrotomy, which entails grabbing the material, placing it in an Endo bag, and extracting it through a 10-mm camera port.[11] Laparoscopic surgery is another option, but it can sometimes be time-consuming and technically difficult. Medical treatment, such as enzyme therapy with papain, cellulase, or acetylcysteine, may be tried, albeit usually ineffective. Non-operative treatments are discouraged due to their high failure rate.[4, 7]

Due to the disease's rarity, there is currently no gold standard treatment; however, patient outcomes and safety should be considered before executing the surgery.

Conclusion

Trichobezoars are uncommon. However, they should be evaluated as a differential diagnosis in young females with vague upper abdominal complaints and an epigastric lump. Radiological examinations could shed light on the problem. Complications are common but can be prevented by carefully detecting and treating a trichobezoar. Recurrences are also well known. These repercussions, such as bleeding or perforation, can be avoided by early detection, and counselling can avert recurrences.

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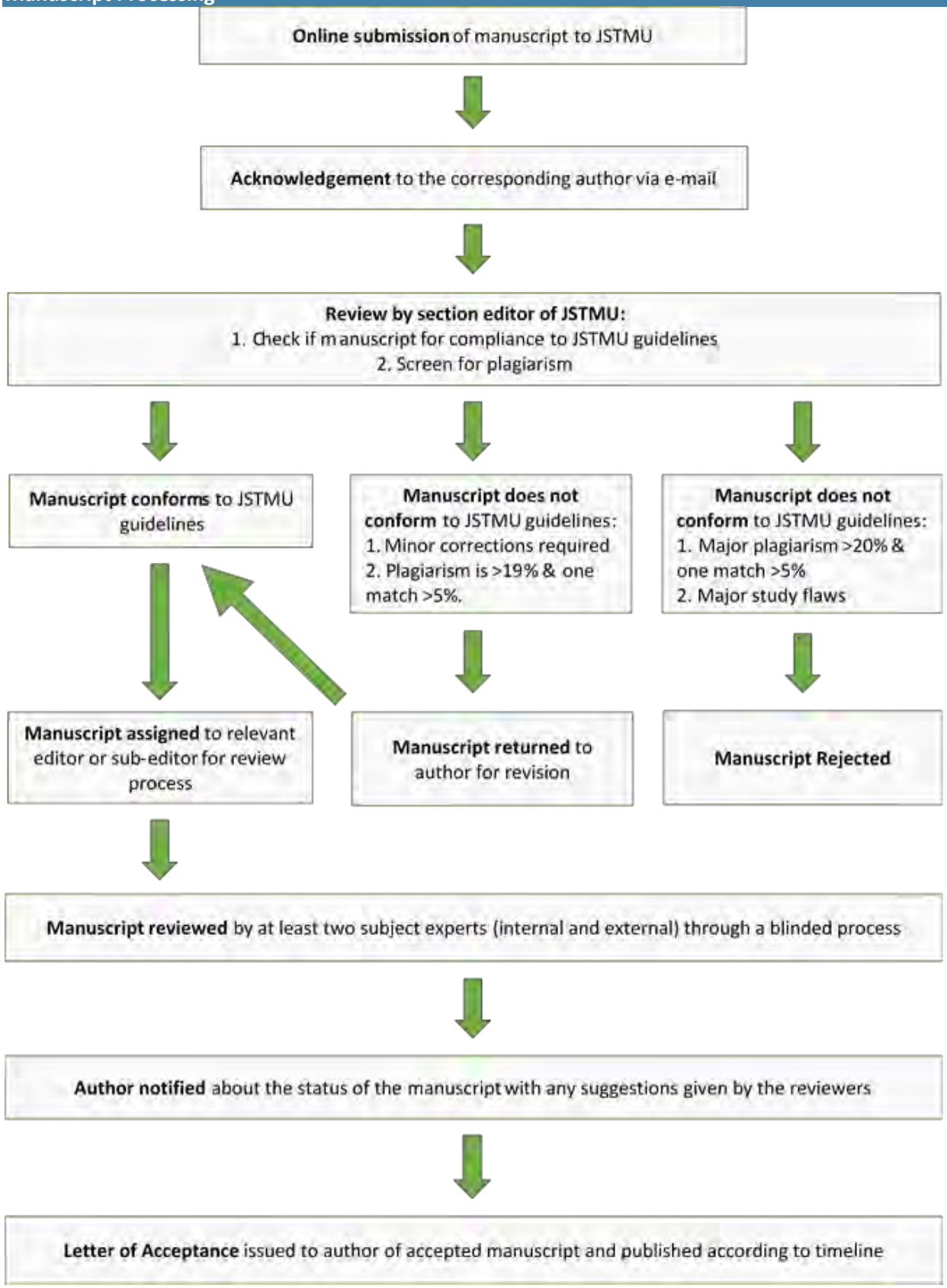

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6. Data analysis

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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Journal of Shifa Tameer-e-Millat University
Editorial Office, 72-Jaffer Khan Jamali Road, Sector H-8/4, Islamabad.
Ph #: +92-51-8438061-65, Ext (110)
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Website: https://j.stmu.edu.pk

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